SCIENCE

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RESEARCH AND THE INDIVIDUAL[1]

By Dr. WM. de B. MacNIDER

KENAN RESEARCH PROFESSOR OF PHARMACOLOGY, THE LABORATORY OF PHARMACOLOGY, UNIVERSITY OF NORTH CAROLINA

THIS is a worthwhile occasion. Twenty-five years ago the North Carolina Chapter of the Society of the Sigma Xi made its appearance at this university. The chapter was installed on the evening of May 6, 1920, under the national presidency of Professor C. E. McClung.[2]

This anniversary occasion is enhanced and made especially appropriate by the fact that during the present year the University of North Carolina is in the process of celebrating its sesquicentennial. During this period of one hundred and fifty years the university has cause to rejoice in the scientific accomplishments and trends which it has given by thought through research to the nation and areas beyond the seas.

A review of the Scientific Bibliography[3] of the university since 1795, prepared some years ago by Mrs. C. Dale Beers, of the Department of Botany, impresses one with the sincere interest which instructors at this institution have had in gaining understanding of a scientific order, of the physical difficulties which must have beset such investigations and the will within

[1] An address on the occasion of the twenty-fifth anniversary of the founding of the North Carolina Chapter of the Society of the Sigma Xi, June 7, 1945.

[2] Wm. deB. MacNider, "Sigma Xi. Half-Century Record and History 1886–1936." North Carolina Chapter, p. 716. Free Press Interstate Printing Corporation, Burlington, Vermont.

[3] Alma Holland (Mrs. C. Dale Beers), *Jour. Elisha Mitchell Scientific Society*, 50: 303, 1934.

such men to live at a level of university understanding through research. The desire to understand the unknown and the will and sacrifice to gain such information is the spiritual inwardness of university life. Such a spiritual inwardness of poise and satisfaction has enabled this life to persist during periods of neglect and the transitory upheavals of educational reformers. Curricula come and go through changes in an attempt to meet an expanding knowledge and educational emergencies of an applied order. Their binding power to reality as they change is only assured through the accomplishments of research. Through it they may find a foothold of factual surety upon which they may rest and to which they may tie. Such research may keep the workshop order of education from becoming a sweatshop type and may, through biological time, helpfully relate the "New Deal" to an ever-changing social environment.

Here in Chapel Hill at our university we take justifiable but never boastful pride in the fact that with the commencement of its being, when a classical order of instruction was usual, certainly the natural sciences were given an important place in the plan for instruction. Joseph Caldwell, the first president of the university, was born in 1773, graduated from Princeton when only 18 years of age and came to Chapel Hill as professor of mathematics at the age of 23. At the age of 31 he became president of the university.[4] In 1824 the trustees of the university gave him $6,600 with which to go to Europe and purchase books and laboratory apparatus. It appears this money was about equally divided between these two sources for purposes of instruction.[5,6] The equipment was chiefly astronomical instruments and consisted in a meridian transit, telescope, a refracting telescope, an altitude and azimuth telescope, a good clock, which is now in the office of President F. P. Graham, a sextant, a Hadley's quadrant and a portable reflecting circle. Certain of these instruments are in the keeping of the Department of Physics and are in some measure usable. The spending of approximately $3,300 by this institution for scientific instruments in the year 1824 gave physical expression of the university's concern for science. This interest has persisted with the years. President Caldwell's interest must have exalted itself into an enthusiasm, for in 1830–31 he caused to be constructed at his own expense, to the amount of $430.29½, at a site near the university campus, a brick astronomical observatory. This was one of the first, if not the first, building erected specifically for astronomical observations in North America. The first recorded use of such instruments was made by Bishop James Madison at the College of William and Mary. In November, 1780, he sent to David Rittenhouse, of Philadelphia, observations on the eclipse of the satellites of Jupiter.

This forwardness in and appreciation of scientific research has continued at the University of North Carolina, not as an organized and regimented undertaking, but as an essential part of the durably satisfying life of the institution. It has asserted itself as a success in the silences through the toil of instructors and a limited number of students who have been willing with a relish to give up certain transitory incidentals and become fastened to learning through investigation. A monastic order of life has not encased such individuals and yet in the simplicity of the lives of certain of these men, in the sparse equipment of their workshops, this order of devotion has shown itself. This is as it should be. Thoughtfulness, which is the touchstone for any research, for the development of a plan to test the truthfulness in the thought, encounters certain difficulties in the hum of a laboratory organized for the mass production of this commodity; research, for immediate results. Such a rush of fulfilment may come later and be effective, but the commencement of such things relishes the quiet room and a peace which permits inquisitiveness. Such a concept has nothing of arrogance or superciliousness in it. It is not in favor of that order of individual who cares

> . . . to dwell remote, aloof
> In some high mansion, built on Wisdom's hill;
> Thence watch the errant crowd go to and fro,
> Matching their wits, striving for precedence,
> Toiling and moiling, hurrying night and day
> To rise to fortune and possess the world.
>
> —Lucretius, ii. 7.

It would, however, emphasize the value of detachment for thought of a logical and analytical order and the deep and lasting satisfaction which may come through discovery made possible by self-denial and toil in the silences in order "to strive, to seek, to find and not to yield."

Research-mindedness is a quality an individual must possess to further his inquisitiveness and gain information by investigation. Just how this order of mind is acquired and developed is difficult to determine. Likely through heredity, as has been the case with the Darwins and the Haldanes and other families, a few individuals are born with it and as their academic training progresses, it becomes of their nature not to be satisfied with the statements of others but to doubt, to inquire and be willing to express such misgivings by tests which they can put into operation in order not only to satisfy their own curiosity but in the hope of being able to add something to a given domain of

[4] Prior to Caldwell's presidency the administration of the university was in the hands of certain members of the faculty, designated "Presiding Professors."

[5] Willis I. Milham, "Early American Observatories." Williams College, Williamstown, Mass., 1938.

[6] Samuel Alfred Mitchell, *Proc. Amer. Philosophical Soc.*, 86: 13, 1942.

knowledge. Investigators by such a nature are the exception. In general such people are made, not just born, and the commencement of their research-mindedness may be due to a something they receive from one or more instructors. Such an instructor is the university order of teacher, without which there is no university. By the technique of his approach in gaining understanding as well as by his life, he likely all unconsciously gives that spark to a student which, fanned by the student's zeal, becomes the light which guides and leads him along pleasant but difficult paths of discovery. He follows these paths freely as an individual and not as a cog in a mechanized unit. For a few, there may be in store some outstanding discovery which will bring with it immediate recognition but for the average individual lost in research, concerned perhaps with the infinitesimally small, these signs of recognition may not come with such a readiness. The research-minded order of scholar finds a deeper satisfaction than surface recognition in the realization that no matter how small his discovery, he has taken his place forever in a composite oneness of understanding by finding a fact regardless of its minute or expanding nature. This order of inward satisfaction sustains and makes content the life of the research individual. It is a communal feeling of this nature which should hold the members in each chapter of the Society of the Sigma Xi and make them, as was the intent of its founders, "companions in zealous research." Progress in research can only come about through the activity of this order of free individual who has a thought and proceeds to follow it. The ability to follow it in its many ramifications depends primarily upon the individual's energy and specialized training. But all too often the nature of the problem fails to confine itself to one category of understanding, the division in which the investigator has had his training. The problem wanders from one area of understanding to another as it seeks to express itself perhaps as life. Group research becomes necessary. Individuals of varied disciplines must come together in order to unravel a variety of complexes which make up the problem as a whole. The structural biologist requires a biochemist, and the biochemist the chemical physicist. The agents of research in such groups must retain their individuality. Should this become lost, the completeness of the research project will fail to find its end reaction and—of even more significance—chance observations, leads, which may be of more importance than the original problem may be overlooked.

The concept of research as an individualistic expression of thought is not in conflict with mass production through research. Such composite research endeavor is necessary for industry and it may be obligatory for life as has been recently demonstrated in such a superb fashion for penicillin under the guidance of the Office of Scientific Research and Development of the National Research Council. Even in this instance, the great discovery which made necessary group activity came from one individual who made an observation and, of most importance, had a thought.

In order for thoughts arising through reason to express themselves by research, the trained individual requires money for his livelihood and for his investigations. But not too much money. Such an agent finds a sufficiency of life outside of the laboratory in rather simple and not too costly adventures. Too much money may separate this order of mind from its labor through the intervention of assistants. A process of weaning commences from the peace and poise of the laboratory to those things secured by money, often only of transitory interest and which lack values of enduring satisfaction. A satisfactory living and a fairly adequately equipped laboratory are necessary for sustained effort. Above all, for that peace of mind which is essential for work and the protection of a family, the certainty of fair compensation when the work days grow shorter and the evening shadows begin to lengthen. Parts of this statement may sound more romantic than real. There is a modicum of sense in it. Much money and those things which it can purchase can only be used and with difficulty enjoyed in an environment strange to and other than the laboratory. The sustaining charm of thought and discovery are in truth masters of the laboratory, and these are of their nature opposed to luxury and are self-sufficient. They partake of naturalness, that difficult-to-obtain and illusive attribute of the human being. This order of research-minded individual finds, as did Lessing, and as demonstrated by the life of Professor John J. Abel, that

> the value of a man is not measured by the truth he possesses, but rather by his sincere effort to discover truth. For it is not through possession of truth, but much more by search for it that his powers are widened, those powers which conduce to evergrowing perfection. Possession makes for tranquility, laziness and conceit. If God, holding in His right hand the complete embodiment of truth and in His left the unswerving and ever-alert search for truth, even though this search be frought with a constant and unremitting erring, should say to me "Choose!" I would humbly embrace His left and say: "Father, give! for the real truth is Yours alone."

And now may I say to the initiates of this evening, as we proceed with this celebration of our twenty-fifth anniversary, that we welcome you, both heartily and earnestly, as research individuals into this company of scholars—The Society of the Sigma Xi.

PROTEIN CHEMISTRY AND MEDICINE[1]

By Professor VINCENT du VIGNEAUD
CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK CITY

WE have heard over and over again of the great contributions that the chemist has made to the well-being of our people through his contributions to medicine. These are gratifying successes and the chemist has a right to be proud of them. However, not all the attempts of the chemist to contribute to medicine have been crowned with success. There are many problems which are badly in need of solution, and upon which the chemist has worked but to date has not entirely succeeded. I should like to take one sector of the field of biochemistry in relation to medicine and spend a few minutes discussing an example or two of the unsolved problems. For isn't it essential for us to evaluate our failure as well as our successes? In considering chemistry's effort to help medicine, we can best appreciate the need of highly trained chemists—and more chemists—to continue the attack on such problems. When a field such as chemistry has not been able to provide medicine with a necessary drug, or an understanding of a particular biological process, or the fate of a substance in the body, or the structure of a certain compound, or a method of analysis for a particular constituent of the body, it usually means that somewhere along the line some piece of fundamental knowledge has been lacking. In order to obtain this knowledge, more fundamental research is absolutely necessary.

Now, then, what are some of these unsolved problems I am talking about? Well, let us consider a very important hormone which you have all heard about. I am thinking of insulin, the hormone which is essential for the utilization of sugar by the body, and which, as you know, is used medically in the control of diabetes. The chemist has done a creditable job of getting this hormone out in pure form and has contributed greatly to many aspects of the chemistry of this important compound; but chemists the world over for twenty years have tried to solve the riddle of insulin. Still we don't know why it possesses its remarkable physiological properties and how it brings about its miraculous effect.

We know that it is a protein, that is to say, that it is a very complex structure made up of many small building blocks, called the amino acids. But somehow the clue has eluded us as to how and why this substance can regulate the amount of sugar in the blood. Furthermore, it has defied synthesis! Why is this? Some will say, of course, that it is impossible to synthesize a protein and therefore it is impossible to synthesize insulin. Are we going to accept that? Of course not! But, if there is to be any hope of ever accomplishing the synthesis of insulin and of truly understanding its chemistry, we must start much further back, and must seek to understand more fully the fundamental chemistry of proteins. For this is the type of problem in which no one knows what the answer might be, nor from what direction the answer might come.

Just as insulin is elaborated by the pancreas to regulate sugar utilization in the body, a series of other proteins are elaborated by the pituitary gland to control various physiological mechanisms. For example, one of these proteins influences the mammary gland, another stimulates the thyroid, another affects the sex glands, and still another is vital for growth. These as well as other protein hormones all present problems similar to those mentioned in connection with insulin.

Akin in some respects to the problem of the chemistry of insulin and the other protein hormones is another problem, that is the chemistry of viruses, some of which have been shown to be a type of especially huge protein molecule. The solution of this problem is of particular importance to the advancement of medicine because viruses are causative agents of many diseases. Problems still more baffling than those posed by the protein hormones are here encountered. How does this particular type of protein multiply in the body? Furthermore, how can this multiplication be hindered? Perhaps in this way, some of the virus diseases might be counteracted. Even though brilliant contributions have already been made by virus chemists, many vitally important questions are yet to be answered.

There are still other proteins which possess remarkable properties the understanding of which is of importance to medicine. For instance, there is a protein of the blood which forms the blood clot, but just what change takes place in the protein during the formation of the clot, and exactly how the transformation takes place, remain to be worked out. There are other proteins in the blood likewise playing vital roles. It is the proteins of the blood, such as the albumin and globulin, that counteract the shock resulting from wounds. It is the need for these proteins that has made collection of human blood so important in the war effort. Other proteins in the blood, present in much smaller amounts, afford the body protection against many diseases such as measles and influenza. These are the so-called antibodies

[1] Talk given during the intermission of the New York Philharmonic-Symphony United States Rubber broadcast on Sunday, February 25, 1945.

which confer on an individual immunity towards certain diseases. These intricate immunological processes abound in problems challenging the chemist and demand more fundamental knowledge of proteins. The same could well be said for enzyme chemistry, which involves an almost countless number of proteins which, at times in conjunction with the vitamins, possess remarkable catalytic powers.

Finally, I might point out that the whole process of the formation and breakdown of the host of proteins in the tissues within the body is still to be worked out. I need not point out that our skin and flesh and internal organs consist mainly of proteins, to have you realize how important protein chemistry becomes to the comprehension of the nature of the repair of tissues, of the healing of wounds, and of the many disease processes and even to the understanding of cancer.

I think that it is evident that more chemists—and even more highly trained chemists—will be needed in the years to come to carry on with these and other problems with their brother scientists in other fields, in order to afford the fundamental basis for still further advances in medicine and thus to help the doctor in his conquest of disease.

As we plan for the future, we must realize that it is easier to appreciate the need of scientific research directly connected with a practical application. It is harder to grasp the need of true fundamental, pioneering research. The type of research I mean is that required to solve that kind of problem of which we have been speaking, where no one knows what the answer may be or from what direction the answer may come.

In whatever planning and organization we may carry out in the postwar years, we must make very sure that we provide to scientists not only the facilities for fundamental research, but we must be very careful to preserve that type of environment which provides the complete freedom for the "playing" of his "hunches" and which allows him to travel without hindrance the pioneer trails that his curiosity beckons him to follow.

In thinking specifically of medicine, I might point out that medicine does need chemistry and chemists for the building of the medicine of to-morrow. The field of medicine to-day has assimilated the biochemistry and physiology of yesterday; and the biochemistry and physiology of to-day must be encouraged along fundamental lines to build the medicine of to-morrow. We can see in retrospect what chemistry has done for medicine, but it is so much harder for the human mind to grasp that the chemistry of to-day and to-morrow will likewise yield discoveries that will be of aid to the medicine of the future.

OBITUARY

LEON HATCHIG LEONIAN
1888–1945

AFTER an illness of sixteen months Dr. Leon H. Leonian, professor of mycology and mycologist in the Agricultural Experiment Station, West Virginia University, died on June 7 at the age of fifty-seven years. He remained active in his work until a month before his death.

He was born at Van, Armenia, on February 27, 1888, the son of Hatchig and Anna Leonian. He left Van after completing his secondary education, and after some journeys into Russia, Egypt and Greece, he came to the United States at the age of twenty. After several years in New York and Detroit he entered the University of Kentucky, from which school he received the B.S. degree in 1916. He then entered the University of Michigan for graduate training and received his M.S. degree in 1917. The following year he was assistant research horticulturist in the Experiment Station at Clemson College. He then went to New Mexico as assistant professor of botany and plant pathology in the New Mexico State College and Experiment Station. He later returned to the University of Michigan, where he studied mycology under Kaufmann; he received the Ph.D. degree in 1922. In that year he came to West Virginia University as assistant plant pathologist in the College of Agriculture and the Experiment Station. After various promotions he was made professor of mycology and mycologist of the station in 1936.

He established an international reputation in three distinct fields of science—plant diseases, the physiology of fungi and in plant breeding. The first phase of his life's work was devoted to the study and control of plant pathogens, particularly the downy mildew parasites, the Fusarium wilt and a wilt of peppers. As he studied the disease-causing organisms he was led gradually to the recognition of the mutability of fungi and to the influence of environment upon the life and character of microorganisms.

His well-known work on the taxonomy of the genus Phytophthora further increased his interest in physiological studies, and this second field of interest became so engrossing that it motivated his research program for the past fifteen years. Even as a graduate student he was primarily interested in understanding the conditions governing the life, growth and reproduction of microorganisms. During the last decade his

interest was fixed on the influence of growth and sexuality factors for fungi and growth factors for bacteria. To these problems he brought a shrewd and penetrating mind and a great persistence in overcoming difficulties. Whenever possible his method of attack was direct, and nothing pleased him more than the successful use of a simple demonstration to establish some fundamental finding.

His third field of science brought him much pleasure and many friends in other than academic circles. His avocation was the growing, improving and breeding of delphiniums, day lilies and oriental poppies. To this enterprise he gave the name "Lyondel Gardens," and in the flower season it was one of the show places of Morgantown. He delighted in showing his treasures to those who appreciated them. He was a speaker of reputation before garden clubs.

For many years he was editor of the Delphinium Year Book, and in 1935 published a book entitled "How to Grow Delphiniums."

He will be remembered by his students as a teacher and as a man who understood their problems. Many students came to him for counsel and help. And in an unobtrusive way he performed many kind deeds which he hid as best he could. His colleagues will miss his example and his determined stand for those things he considered right and just. His friends have indeed suffered a grievous loss. A student loan fund has been established by friends and associates in his memory.

He is survived by his widow, Mrs. Nell Lanham Leonian, and three sons, Phillip, Armen and John. In addition, two brothers and a sister survive in the Armenian Republic of the U.S.S.R.

C. R. ORTON

RECENT DEATHS

DR. NEVIN M. FENNEMAN, until his retirement in 1937 with the title emeritus, professor of geology and geography at the University of Cincinnati, died on July 4 at the age of seventy-nine years.

DR. DANIEL ROCKMAN BERGSMARK, associate professor of geography at the University of Cincinnati, died on June 25 at the age of forty-six years.

THE death on June 24 at the age of sixty-eight years is announced of Dr. Arthur W. Walker, professor emeritus of bacteriology of Northwestern University.

EDITH REBECCA SAUNDERS, formerly fellow and director of studies in the natural sciences at Newnham College, Cambridge, died on June 4 from injuries received in a motor accident.

SIR PETER CHALMERS MITCHELL, F.R.S., secretary to the Zoological Society of London from 1903 to 1935, was struck by a taxi-cab on June 29 and died on July 2 from the result of injuries received.

SCIENTIFIC EVENTS

THE GERARD SWOPE FOUNDATION OF THE GENERAL ELECTRIC COMPANY

To assist in higher education and fundamental research work in scientific and industrial fields, a fund of $400,000 has been set aside by the directors of the General Electric Company to be known as the Gerard Swope Foundation. Mr. Swope served as president of the company for more than nineteen years, from May, 1922, until the close of 1939, and for an additional two years in 1942–44 he returned to head the company when C. E. Wilson, now president, was acting as executive vice-chairman of the War Production Board. When he resigned at the close of 1944, Mr. Swope had also served as a director of the company for more than twenty-two years.

The new foundation was created "as an expression of appreciation of Mr. Swope's great contribution as the leader and inspiration of the General Electric Company for so many years, and as a means of making this appreciation of enduring and constructive benefit to the company and to the electrical industry."

It is proposed to utilize the income of the foundation in the following ways:

In granting loans or scholarships to employees and to the children of present or former employees of the company and its affiliated companies, to help them pursue their work in any field of study and in any approved university, college or technical school in the United States that they may select;

In granting graduate fellowships to the same classifications of individuals to be used by the recipient for graduate work in industrial management, engineering, the physical sciences and in any other scientific or industrial field;

In granting loans, scholarships or fellowships in any of the above fields to any other person that may be deemed worthy of assistance;

And finally, in granting graduate fellowships, to make contributions to the university, college or technical school to help in defraying the cost of equipment and material, especially needed in connection with a research project.

Applicants for loans, scholarships and fellowships will be considered not only from the standpoint of academic attainment and financial needs, but also from the standpoint of character and personal qualifications for deriving the greatest good from the continuation of their studies. The grants will be made without regard to sex, color, creed or national origin.

THE CANAL ZONE BIOLOGICAL AREA

THE trustees of the Canal Zone Biological Area held their annual meeting in the building of the National Academy of Sciences on June 12. Among other things they took action to enlarge the availability of the area's Barro Colorado Island to industrial research laboratories and others interested in research or testing under tropical conditions.

The Canal Zone Biological Laboratory is an agency set up by the Congress to administer Barro Colorado Island in Gatun Lake and other tropical areas which may be designated as permanent primeval sites for biological and other research. The directors are the president of the National Academy of Sciences, *Chairman;* the secretary of the Smithsonian Institution, *Vice-chairman;* the Secretaries of War, Interior and Agriculture, and three distinguished biologists appointed by the president of the academy. At present these latter are Dr. Thomas Barbour, Harvard University; Dr. E. D. Merrill, director of Arnold Arboretum of Harvard University; and Dr. Remington Kellogg, of the U. S. National Museum.

Barro Colorado Island is a large island of virgin tropical forest in Gatun Lake which is rich in species of tropical flora and fauna. Originally it was a hilly section of the forest which became an island when the lake was formed. It is unique in that while it is a wild tropical jungle it is easily accessible to the facilities of modern cities.

From the day it was formed Barro Colorado has been preserved and used as a tropical laboratory—first under private auspices and later as a government monument set aside by Act of Congress in order to preserve its unique characteristics. It is equipped with laboratories and living quarters and is within twenty minutes by boat of a station on the Panama Railroad.

While set aside primarily for biological research, other kinds of research and testing under humid tropical conditions have been carried on. This has been particularly the case during the war period. The work has ranged from problems of deterioration of equipment, clothing and packaged goods under tropical conditions, to those of sound and radio transmission in tropical jungles.

These experiences have satisfied the directors that a certain amount of such work can be continued regularly in connection with the primary purpose for which the area was established. They have consequently authorized setting aside a small area near the laboratory for such use. Information as to the conditions governing such work can be obtained by writing to the office of the Canal Zone Biological Area, care of the National Academy of Sciences, 2101 Constitution Avenue, Washington 25, D. C., or to that of the executive officer, Dr. Alexander Wetmore, Smithsonian Institution, Washington 25, D. C.

THE ISOTOPE RESEARCH COMMITTEE

A CONFERENCE of research workers interested in the use of carbon isotopes for biochemical and biological studies was held on June 19 and 20 at the Lankenau Hospital Research Institute in Philadelphia.

On the first day reports of current work in this field were presented by Major Allan Hemingway and by Drs. E. A. Evans, D. Rittenberg, D. W. Wilson, M. Cohn, G. Medes, S. Weinhouse and M. D. Kamen. Descriptions and demonstrations of the latest developments in the production, concentration and measurement of the carbon isotopes were presented by Drs. A. O. Nier, J. R. Dunning and A. Reid (Columbia University).

The second day was devoted to a discussion of the available facilities for carrying on biochemical studies. The afternoon was spent at the laboratories of the Houdry Process Corporation of Pennsylvania at Marcus Hook to inspect their mass spectrometer and their thermal diffusion plant for concentration of C–13.

A national committee was formed for the purpose of sponsoring and aiding biochemical research with carbon and other isotopes by institutions and responsible individuals. The Isotope Research Committee consists of a biological and a physical section. The latter is to act primarily in an advisory capacity to the biological section.

The members of the sections are as follows:

Biological Section

D. W. Wilson, *Chairman,* University of Pennsylvania
E. A. Evans, University of Chicago
A. B. Hastings, Harvard University
A. Hemingway, University of Minnesota
M. D. Kamen, Washington University
G. Medes, Lankenau Hospital Research Institute
D. Rittenberg, Columbia University
V. du Vigneaud, Cornell University
S. Weinhouse, Houdry Process Corporation of Pennsylvania
G. H. Werkman, Iowa State College

Physical and Chemical Section

A. O. Nier, *Chairman,* University of Minnesota*
E. J. Booth, Columbia University
J. R. Dunning, Columbia University
A. V. Grosse, Houdry Process Corporation of Pennsylvania

The secretary of both committees is Dr. Stanley P. Reimann, of the Lankenau Hospital Research Institute.

It was agreed that a symposium, covering both the physical and biological aspects, would be particularly useful at the present time and that another meeting be held within the next year to see what progress has been made.

* At present at the War Research Laboratories of Columbia University.

PROMOTIONS IN THE UNIVERSITY OF CALIFORNIA AT BERKELEY

THIRTY-THREE members of the faculties of the University of California have been promoted to full professorships; thirty-four have been made associate professors, and thirty-two have been given assistant professorships.

At Berkeley, promotions in the sciences are as follows:

Professorships: E. W. Gifford, anthropology; R. W. Jeans, architecture; A. S. Foster, botany; L. C. Marshall, electrical engineering; C. J. Vogt, mechanical engineering; C. B. Morrow, mathematics; Miriam Simpson, anatomy; P. L. Kirk, biochemistry; I. L. Chaikoff, physiology; R. C. Tryon, psychology; A. H. Miller, zoology; T. E. Rawlins, plant pathology, and G. J. Seaborg and R. S. Pitzer, chemistry.

Associate professorships: Melvin Calvin, chemistry; L. J. Black, electrical engineering; Alfred Tarski, mathematics; L. A. Strait, biophysics; A. L. Foster, mathematics; H. R. Josephson, forestry; H. A. Barker and W. Z. Hassid, plant nutrition; E. M. Mrak, food technology; Helen L. Gillum and Catherine Landreth, home economics.

Assistant professorships: E. A. Steinhaus, bacteriology; H. W. Iversen and P. C. Nelson, mechanical engineering; L. A. Swinford, mathematics; M. W. Morgan, Jr., optometry; W. E. Hazen, physics; A. E. Michelberger, entomology and parasitology, and P. R. Day, soils.

THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH

THE Board of Scientific Directors of the Rockefeller Institute for Medical Research announces the promotion of Dr. Charles L. Hoagland from associate member to member.

Other promotions and new appointments are as follows:

Promotions: From associate to associate member, Dr. Lyman C. Craig, Dr. Lewis G. Longsworth and Dr. Theodore Shedlovsky. *From assistant to associate member,* Dr. Paul B. Hamilton and Dr. C. Arthur Knight, Jr.

New appointments: Associate member, Dr. Henrik Dam; *Associate,* Dr. Maclyn McCarty; *Assistants,* Dr. Charles F. Huebner, Dr. Daniel H. Labby, Dr. Gardner Middlebrook and Dr. Gerald Oster.

The board also announces that Dr. Peyton Rous, who has reached the age of retirement, has been made member emeritus of the institute.

SCIENTIFIC NOTES AND NEWS

HARVARD UNIVERSITY at its commencement exercises conferred the degree of doctor of science on Sir Alexander Fleming, discoverer of penicillin, professor of bacteriology at St. Mary's Medical School, University of London; on Dr. Roger Adams, head of the department of chemistry of the University of Illinois; on Frederick E. Terman, head of the department of electrical engineering of Stanford University, now on leave as director of radio research for war at Harvard University; on Dr. Edwin J. Cohn, professor of biological chemistry at the Harvard Medical School and director of blood plasma research during the war; on Dr. Frederick V. Hunt, professor of physics and director of the underwater sound laboratory of Harvard University, and on Dr. A. Baird Hastings, professor of biological chemistry at Harvard University. The doctorate of laws was conferred on Bradley Dewey, formerly rubber director of the War Production Board.

SIR ALEXANDER FLEMING, M.D., was awarded the honorary degree of doctor of science at the convocation on June 18 of the University of Pennsylvania. The degree was presented by Dr. A. N. Richards, professor of pharmacology and chairman of the U. S. Committee of Medical Research, to "the discoverer of penicillin, the most potent weapon yet known to man in the war of science against disease."

DR. WALTER S. ADAMS, director of the Mount Wilson Observatory of the Carnegie Institution of Washington, was awarded the honorary doctorate of science by the University of Chicago at the spring convocation on June 15. The citation was as follows: "An astrophysicist who discovered a method of determining the distances of the stars from their spectra and who developed spectrographic instruments of high dispersion for the study of the atmospheres of the stars."

THE degree of doctor of science was conferred at the commencement of Hunter College, New York City, on Dr. Margaret Barclay Wilson, professor emeritus of physiology and hygiene.

DR. JOSEPH W. BARKER, of New York, who has been special assistant to the Secretary of the Navy since before Pearl Harbor and who has been largely responsible for the establishment of the highly successful training programs of the Navy, has received the Distinguished Civilian Service Award. The presentation was made at a special ceremony by Ralph A. Bard, Under Secretary of the Navy. The citation reads: "Through his energy, ability and tact, he contributed in an outstanding manner to the formulation of basic personnel policies and to the highly successful cooperation between the armed services in matters of personnel administration. Through his services Dr.

Barker rendered a distinguished contribution to the Navy and to his country in time of war, which rightly deserves the Navy's highest civilian award." Dr. Barker is returning to his post as dean of engineering, Columbia University.

IN recognition of his work on the various types of Rh factors and on their genetic transmission, the College of Physicians of Philadelphia is awarding on July 14 the Alvarenga Prize for this year to Alexander S. Wiener. Dr. Wiener will give the Alvarenga Lecture before the College of Physicians of Philadelphia and the Philadelphia County Medical Society on October 3, on "Rh Blood Factors in Clinical Medicine." The Alvarenga Prize was established by the will of Pedro Francisco daCosta Alvarenga of Lisbon, Portugal, an associate fellow of the College of Physicians, "to be awarded annually by the College of Physicians on each anniversary of the death of the testator, July 14, 1883." The award is usually made for outstanding published work, and the recipient is invited to deliver an Alvarenga Lecture before the college.

ON the occasion of his retirement after serving for thirty-six years, Dr. John W. Roberts, plant pathologist of the Bureau of Plant Industry of the U. S. Department of Agriculture, was the guest of honor at a banquet given on June 15 by his friends.

HENRY T. HEALD, president of the Illinois Institute of Technology, has been elected president of the Western Society of Engineers.

PROFESSOR W. H. TWENHOFEL, chairman of the department of geology of the University of Wisconsin, who retired on July 1 to become emeritus professor of geology, is spending the summer in Newfoundland, where he is studying the Silurian for the Newfoundland Geological Survey. Dr. Parker D. Trask, of the U. S. Geological Survey, has been appointed professor of geology to carry on instruction in sedimentation, a subject to which Professor Twenhofel has mainly devoted himself.

DR. HARRISON HALE, for the past twenty-seven years head of the department of chemistry of the University of Arkansas, retired on July 1 with the title of emeritus professor of chemistry. Dr. Hale will conduct a survey of the industrial water supplies of Arkansas with the University Bureau of Research. Dr. E. Wertheim, professor of chemistry, will become head of the department.

DR. CARLETON C. MURDOCK, professor of physics at Cornell University, has been elected dean of the faculty. He succeeds Dr. Cornelius Betten, who recently retired. Dr. Murdock has been a member of the faculty of Cornell University since 1909.

DR. SIDNEY J. FRENCH, professor of chemistry at Colgate University, has been appointed dean of the faculty.

WILLIAM I. BOOK, professor of physics at the University of Pennsylvania, who has just attained the age of seventy years, has been appointed professor emeritus. He retired from active duty on July 1. He and Mrs. Book will continue to live in Narberth, Pa., in the house that Professor Book designed and built with his own hands twenty-three years ago. As a tribute to him the Society of the Alumni of the Graduate School of the University invited him to deliver his demonstration lecture on "The Physical Basis of Music" at their annual meeting held on June 27. Professor Book has delivered this lecture to the undergraduates at the close of each academic year for many years.

DR. JOSEPH B. REYNOLDS, professor of mathematics and theoretical mechanics at Lehigh University, has been appointed head of the department of mathematics and astronomy.

AT Yale University Dr. Richard Foster Flint has been promoted to a professorship of geology.

DR. GEORGE A. BURNHAM, associate editor of *The Review of Scientific Instruments,* and for the last three years assistant to the director of the American Institute of Physics, has been appointed associate professor of physics and assistant to the president of Norwich University, Northfield, Vt.

DR. DIO L. HOLL, professor of mathematics at Iowa State College and research professor of applied mathematics in the Engineering Experiment Station, has been named head of the department of mathematics. His predecessor, Dr. Edwin R. Smith, remains as professor in the department.

DR. KENNETH E. CASTER, assistant professor of geology at the University of Cincinnati, who is now on leave as visiting professor at the University of São Paulo, Brazil, has been appointed director of the department of geology-paleontology at São Paulo. Dr. Caster is reorganizing the curriculum in the natural sciences in preparation for the establishment in Brazil of the first school of geology, as a pure science. He is aiding also in plans for forming a Brazilian Geological Society and is directing field studies of Devonian-period fossils in that area.

DR. EDWARD G. BAYFIELD has resigned as head of the department of milling industry of the Kansas State College to become director of products control and research for the Standard Milling Company. His new address will be 309 West Jackson Boulevard, Chicago 6, Illinois.

THE National Society of Sigma Xi has made an award of $300 to Dr. Josiah L. Lowe, of the New York State College of Forestry at Syracuse University, for the purpose of aiding in a taxonomic study of the pore fungi of the eastern United States. He will make a further study of the classification and the relationships between various species of these organisms which cause rot in lumber and other products of the forest. The material accumulated by Dr. Lowe will be used in the preparation of a manual on the subject which will be published by the New York State College of Forestry.

DR. RALPH W. HEINKAMP, professor of chemistry at the University of Rochester, will leave soon for Germany on a mission for the Army and the Office of Scientific Research and Development.

DR. IRVINE H. PAGE, director of the Research Division of the Cleveland Clinic Foundation, addressed on May 10 the Hollywood Academy of Medicine on "The Nature and Treatment of Hypertension," and the School of Aviation Medicine at Randolph Field on May 6 on "The Mechanism and Treatment of Shock."

THE annual A. C. Helmholz Lecture at the University of Wisconsin was delivered on June 1 by Dr. Thomas Duckett Jones, assistant professor of medicine at the Harvard Medical School. His subject was "Rheumatic Fever."

THE fiftieth annual installation of new members was conducted on June 8 by the University of Minnesota Chapter of the Society of the Sigma Xi. At this meeting Dr. Owen H. Wangensteen, head of the department of surgery of the School of Medicine and president of the chapter, discussed "The Graduate Student and Research." Forty new members were initiated.

THE third Inter-American Conference on Agriculture will be held at Caracas, Venezuela, opening on July 24, for a period of approximately two weeks. The primary objective of the discussions will be to survey the problems affecting agriculture in the postwar period. The *Experiment Station Record* reports that a series of technical bulletins is being prepared by Venezuelan authorities on agriculture and animal husbandry. The U. S. Department of Agriculture is cooperating in the preparation of documentary material as well as a bulletin of information on agriculture in the United States, which will be available for public distribution in Latin America after the conference.

NATIONAL INSTITUTE OF HEALTH research fellowships are being set up under the Public Health Service. They offer opportunities for study and research with specialists in the chosen field of the student at the institute or in some other institution of higher learning. The junior research fellowships will be awarded to those holding masters' degrees in the sciences allied to public health from an institution of recognized standing. They will receive $2,400 per annum. The senior research fellowships are for those holding a doctorate degree in one of the sciences allied to public health. Senior fellows will receive $3,000 per annum.

AN executive order, providing for the release of scientific information, was signed by President Truman on June 8. To determine what should be released for publication, the director of War Mobilization and Reconversion, according to *Chemical and Engineering News,* is authorized to review all scientific and technical information and recommend release. To assist the director an interdepartmental board, a Publication Board, has been established, consisting of the director as chairman, the Attorney General, the Secretary of the Interior, the Secretary of Agriculture, the Secretary of Commerce and the Secretary of Labor. The Secretary of War, the Secretary of the Navy, the director of the Office of Scientific Research and Development and the chairman of the National Advisory Committee for Aeronautics may designate one liaison officer each, who may attend meetings and participate in discussions of the board. Committees of civilian employees of the Government and of officers of the Army and Navy may be set up to assist in the work.

A RESOLUTION was adopted on June 22 at the quarterly meeting of the New England Council appealing to the Congress to grant draft deferments to scientific and technical students and correct a situation "which has already placed this country at a disadvantage compared with other Allied Nations and promises if continued to be destructive to postwar prosperity" in the industrial United States. It is pointed out that Selective Service was "creating a dearth of young American scientists and engineers, and that "both Great Britain and Russia had continued throughout the war the policy of deferring such young men."

THE name of the Spencer Lens Company, of Buffalo, N. Y., was changed on June 30 to the American Optical Company Scientific Instrument Division. For ordinary purposes the firm will still be known as the Spencer Lens Company.

AT an annual conference on April 12 and 13 of the X-ray Analysis Group of the British Institute of Physics and of the Conference on X-rays in Industry, Sir Lawrence Bragg discussed the conclusions of a sub-committee on publication. According to *Nature,* he reported that there is at present no journal dealing satisfactorily with the interests of the group, and

papers on crystallographic subjects appear in nearly sixty different periodicals. The committee is satisfied that there are enough British papers yearly to make possible the publication of a quarterly journal. The scope of the journal would be determined by the material investigated, not the methods used; that is, it would cover structure of matter, not diffraction. The American Society for X-ray and Electron Diffraction is discussing a similar project, and cooperation with them might be arranged. The possibility of cooperating with continental workers is also under consideration. The conference expressed its general approval of a new journal and authorized the committee to continue with the project.

PROFESSOR W. J. LUYTEN, of the University of Minnesota, and Martin Dartayet, Cordoba, Argentina, announce the discovery on June 16 of a new white dwarf in the constellation Chamaeleon. They state that the star is of the seventeenth photographic magnitude, and thus by far the faintest white dwarf known. It has a proper motion of 0".57 annually in a direction of 308 degrees which suggests that the star is comparatively near and some 40,000 times less luminous than the sun. This in turn implies that the star is probably not much larger in size than the moon, and must have a density of the order of 10,000,000 times that of water or more than one hundred tons per cubic inch.

THE CASE SCHOOL OF APPLIED SCIENCE held on June 6 a symposium on "Mathematical Analyzers and their Applications in Industry." Included among the speakers, and their subjects, are Dr. H. W. Bode, of the Bell Telephone Laboratories, "Applied Mathematics in Industry"; Dr. H. A. Travers, of the Westinghouse Electric Corporation, "The Use of the Network Analyzer in the Power Industry"; Dr. Sidney W. McCuskey, of Case School, "Harmonic Analysis and Synthesis"; H. A. Peterson, of the General Electric Company, "Solution of Engineering Problems with the Differential Analyzer," and Dr. Wallace J. Eckert, director of the Watson Scientific Computing Laboratory, Columbia University, "Punched Card Methods in Engineering Computations." At the luncheon meeting, Dr. William E. Wickenden, president of the Case School, acted as toastmaster and Charles A. Kirk, vice-president of the International Business Machines Company, spoke on "The Influence of Machine Calculating Methods on Industrial Progress."

THE Public Health Service announces the establishment of National Institute of Health Research Fellowships after July 1. The junior research fellowships will be available to those holding master's degrees in the sciences (such as physics, chemistry, entomology, etc.) allied to public health from an institution of recognized standing. The stipend will be $2,400 per annum. The senior research fellowships will be available to those holding a doctorate degree in one of the sciences allied to public health. The stipend will be $3,000 per annum. These fellowships will offer an opportunity for study and research in association with highly trained specialists in the candidates' chosen field at the institute or some other institution of higher learning. Letters of inquiry should be addressed to The Director, National Institute of Health, Bethesda 14, Maryland.

THE oil companies of the Shell group have given a capital sum of £435,000 and £2,500 a year to the University of Cambridge for the establishment of a school of engineering and the provision of scholarships.

A REUTER'S dispatch from London states that the French Government has made a grant of 10,000,000 francs to the Pasteur Institute, Paris, to enable it to develop research into the preparation of penicillin.

PROFESSOR R. COURRIER, of Paris, would like to receive reprints from 1940 to date in the field of endocrinology. All reprints may be sent directly either to his address, Collège de France, Rue des Ecoles, Paris 5e, or to Dr. Joseph Schiller, Carnegie Institution of Washington, Department of Embryology, Wolfe and Madison Streets, Baltimore 5, Md., who will forward them. The assistance of his colleagues in the United States would be greatly appreciated.

DR. H. F. CHU, of the department of entomology of the University of Illinois, is collecting reprints on all phases of zoology for the National Academy of Peiping, China. He would appreciate receiving literature in zoology, especially in entomology.

SPECIAL ARTICLES

A FILTER-PASSING AGENT PRODUCING INTERSTITIAL MYOCARDITIS IN ANTHROPOID APES AND SMALL ANIMALS[1]

IN November, 1944, the body of a well-nourished, adult male gibbon was brought to our laboratory because of its sudden and unexpected death. The animal had always been well until one morning it suddenly dropped dead without warning. It had shown no paralysis. An autopsy revealed a dilated heart, pericardial effusion, pulmonary edema and a

[1] From the Laboratory Division, AAF Reg. and Conv. Hosp., Miami Beach, Fla.

bilateral hydrothorax. Histological examination showed an intense diffuse interstitial myocarditis and pulmonary edema. The remaining viscera were negative. The brain showed nothing. The spinal cord was not examined. About six weeks later the body of a 5-year-old, well-nourished, male chimpanzee from the same Anthropoid Ape Research Foundation, was delivered to us. The clinical history was identical with that of the gibbon except that the animal had vomited its breakfast and died very suddenly. The body had been overnight in the refrigerator. At autopsy the same gross and histological findings were observed as in the gibbon. The brain was negative. The spinal cord was not examined.

Fluid from the chest cavity and spleen tissue suspended in saline solution were inoculated into five mice each. All these mice developed paralysis of the hind legs and showed microscopically widespread myocarditis. A mixture of organs from these 10 animals, including lung, heart and spleen, was suspended in saline and inoculated intracranially and intravenously into five more mice. These latter animals were all paralyzed on the 4th day and dead on the 8th day after inoculation. The original chimpanzee chest fluid which had been preserved in the frozen state was again inoculated into 4 mice either intravenously, intraperitoneally or intracranially, and these mice were dead in 6 days following paralysis on the 5th day. All this group showed acute myocarditis microscopically. The organs from this last series were suspended in ascitic fluid and used throughout the remainder of the experiments as a source of the agent. Four mice were inoculated intravenously and intraperitoneally with this ascitic fluid suspension and another group of 4 mice was inoculated with a Seitz filtrate of the same suspension. Those inoculated with the unfiltered suspension were paralyzed on the 4th post-inoculation day and those with the Seitz filtrate on the 5th day. The heart of one of the mice inoculated with the Seitz filtrate which showed very marked myocardial damage was then ground up and suspended in ascitic fluid. Four mice were inoculated with this suspension of heart. One animal showed practically no heart damage, one had mild lesions, and two showed very striking myocardial leukocytic infiltration and necrosis. Heart suspensions in ascitic fluid were made of these hearts separately and then passed through a Seitz filter and injected into 10 mice. All these animals developed marked myocarditis. The material from this strain of hearts suspended in ascitic fluid and Seitz filtered is now regularly producing paralysis and myocarditis in its fifth passage.

Berkefeld filtrates from the organs of mice inoculated with the unfiltered basic mouse organ suspension produced the same typical myocarditis as observed in all previous animals. Five mice were given intranasal instillations with organ, ascitic, saline suspension of mice dying with myocarditis. All the first group developed myocarditis and five other mice were inoculated intranasally with nasal washings of a paralyzed mouse; three of the latter group showed distinct cardiac lesions. The organs of these first animals suspended in ascitic fluid were inoculated intranasally, intravenously and intraperitoneally into 4 mice and all developed paralysis and myocarditis.

Heart, spleen and chest fluid from two chimpanzees dying from other causes were suspended in ascitic fluid and inoculated in the same manner as that employed for the original material, and none of these animals developed any lesions but remained quite healthy and showed no visceral microscopic changes when they were sacrificed.

Four, seven-day, fertile hen eggs were inoculated with 10 per cent. serum-saline suspension of two mouse hearts from a third passage of the original ape chest fluid which had previously been passed through a Seitz filter. These eggs were opened on the third day after inoculation and the markedly hyperemic embryos and membranes were frozen. Later these were suspended in ascitic fluid, ground and passed through a Berkefeld filter. This sterile filtrate has consistently produced myocarditis in 31 mice and in 8 of 11 guinea pigs inoculated. The guinea pigs did not show paralysis.

Five mice were inoculated with a potent strain of the agent, heated to 56 degrees for twenty minutes. Two animals showed paralysis and two showed microscopic myocarditis, although none succumbed to the infection.

Four mice were inoculated with a potent strain of the agent that had been heated to 70 degrees for 20 minutes. Neither paralysis nor myocarditis resulted in these animals.

DISCUSSION

A filter-passing agent obtained from pleural fluid and spleen of a chimpanzee that died from acute cardiac failure and acute pulmonary edema has been passed through a series of 122 mice and has, with rare exception, regularly produced paralysis followed by death or apparent recovery after a week or two. At necropsy interstitial myocarditis has been found in almost all animals. Twenty-five control mice have shown no lesions. In the animals that died during the paralytic stage acute myelitis of the cord was observed. Histologically the lesions in the heart muscle ranged from rather small foci of myocardial

necrosis and interstitial leukocytic infiltration to extensive and widespread areas of necrosis and inflammation. In those animals that recovered from their paralysis and appeared to be approaching normalcy, the microscopic myocardial lesions varied, often showing marked calcification in the zones of necrosis, fibroblastic replacement of muscle and early scar tissue formation. These older lesions were always accompanied, however, by varying degrees of leukocytic reaction.

This filter-passing agent has been found to be sterile on repeated culture. It will withstand heating to 56 degrees C for 20 minutes, losing some of its potency but not its specificity and it is completely destroyed by heating to 70 degrees C for 20 minutes.

Extracts of organs of companion chimpanzees dying of other conditions have uniformly failed to produce any lesions in mice. The agent has been passed through Berkefeld and Seitz filters and has been transferred to seven-day chick embryos and again passed through Berkefeld filters without losing its potency or specificity.

On rare occasions small foci of round cells have been found in the kidneys and the pulmonary lesions range from hyperemia to patchy foci of edema and even occasionally broncho-pneumonia. Splenic hyperplasia has also been observed rather frequently. The other viscera have shown no lesions that could be attributed to the agent.

The agent has been found to be potent and specific when introduced intravenously, intraperitoneally, subcutaneously, intracranially and by intranasal instillations. Moreover, it is found to be present in the nasal washings of inoculated animals. Quite recently it has been employed to produce myocarditis in guinea pigs and rabbits and we are now studying these myocardial changes with the electrocardiograph. This work is still in progress.

The cardiac lesions of this ape disease and sporadic human acute interstitial myocarditis of unknown etiology are strikingly similar.

So far as we have been able to learn, this myocarditis producing agent has not been described previously.

LT. COL. F. C. HELWIG, M.C.
CAPTAIN E. C. H. SCHMIDT, M.C.

VITAMIN-SYNTHESIZING DEFICIENCIES IN YEASTS SUPPLIED BY HYBRIDIZATION[1]

VITAMIN-SYNTHESIZING deficiencies of *S. cerevisiae* can be supplied by hybridizing it with species able to synthesize the vitamins for which it is deficient. Most strains of *S. cerevisiae* are deficient in the ability to synthesize biotin and vary from good to poor in the ability to synthesize pantothenic acid. This species appears to be heterozygous for the genes controlling the ability to synthesize pantothenic acid. Our culture of *S. carlsbergensis* is capable of synthesizing both pantothenic acid and biotin in large quantities, but is unable to synthesize pyridoxine, which *S. cerevisiae* synthesizes well. Haplophase cultures[2] derived from *S. carlsbergensis* were biotin +, pantothenic acid + and pyridoxine –. They were mated with haplophase cultures of *S. cerevisiae*, which were biotin –, pantothenic acid – and pyridoxine +. The hybrid synthesizes all three vitamins in large quantities.

The technique was that developed by Burkholder[3] in his survey of vitamin-synthesizing ability of various yeast species. The standard medium containing glucose and asparagin and various minerals was supplemented with the six B vitamins (exclusive of B_2). In the medium containing the six vitamins, growth was nearly complete at the end of three days. The cultures were grown in $6 \times \frac{3}{4}''$ Kimble test-tubes and the growth was determined by measuring the turbidity with a photoelectric colorimeter. Other nutrient media were made up corresponding to the complete medium described above except that single B vitamins were lacking. Since these B vitamins are essential to cell metabolism, it is assumed that a culture able to produce good growth in a nutrient lacking a given vitamin is able to synthesize this vitamin and that the converse is also true.

TABLE 1

	No vitamins	All vitamins	-pyridoxine	-pantothenic acid	-thiamin	-biotin	-niacin	-inositol
S. cerevisiae diploid	0	315	340	215	306	11	324	300
S. carlsbergensis diploid	1	350	24	280	355	280	340	315
S. cerevisiae haploid	0	309	285	13	290	12	306	230
S. carlsbergensis haploid	3	330	23	204	323	124	322	290
Hybrid	7	303	313	241	314	134	304	282

The amount of inoculum was tested and shown not to carry enough vitamin to obscure the results.

The haplophase segregant of *S. cerevisiae* is pantothenic acid –, while the diploid from which it was derived was pantothenic acid +. This indicates that

[1] This work was supported by a grant from Anheuser-Busch, Inc. St. Louis.

[2] Carl C. Lindegren, *Ann. Mo. Bot. Garden*, 32: 107–123, 1945.

[3] Paul R. Burkholder, I. McVeigh and D. Moyer, *Jour. Bact.*, 48: 385–391, 1944.

the diploid culture was heterozygous for the gene-pair controlling pantothenic acid synthesis.

Table 1 shows the turbidity readings of the original cultures of *S. cerevisiae* and *S. carlsbergensis*, their haplophase segregants and the hybrid. Analysis of the hybrid by dissection of ascospores indicated that it was heterozygous for the ability to synthesize pyridoxine, pantothenic acid and biotin.

S. globosus[4] is capable of synthesizing pantothenic acid, but is incapable of synthesizing thiamin. A hybrid was made with a haplophase from a homozygous pantothenic-deficient culture of *S. cerevisiae* (different from the one used above) and a haplophase culture of *S. globosus*. Several hybrids were produced by this mating, and one of them sporulated well, but only a few of the ascospores were viable. One of the hybrid-haplophases was backcrossed to the original pantothenic-deficient *S. cerevisiae*. The resulting diploid synthesized both pantothenic acid and thiamin efficiently. Since neither parent could synthesize both vitamins, the hybrid had obviously obtained its ability to synthesize pantothenic acid from *S. globosus* and thiamin from *S. cerevisiae*. The hybrid was a poor synthesizer of biotin, but this was according to expectation, since neither parent possessed the ability. The data appear in Table 2.

TABLE 2

	-All	all	-Py	-Pa	-T	-B	-N	-I
S. cerevisiae	8	362	355	50	313	19	355	300
S. globosus	9	270	254	241	26	20	258	250
Hybrid	5	290	293	258	290	15	294	300

These experiments prove that a vitamin-synthesizing deficiency in a yeast can be supplied by hybridization and that the heterozygote usually synthesizes the vitamin nearly as well as the homozygote.

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WASHINGTON UNIVERSITY, ST. LOUIS

STREPTOMYCES ANTIBIOTICS. I. CRYSTALLINE SALTS OF STREPTOMYCIN AND STREPTOTHRICIN

METHODS have been found for securing certain crystalline salts of streptomycin and streptothricin.

These antibiotics are water-soluble, nitrogenous, thermostable, basic organic substances produced by species of *Streptomyces* in suitable culture media. Streptomycin[1] was obtained first in 1944 as a crude concentrate which was prepared from cultures of *Streptomyces griseus*. It is strongly bacteriostatic against gram-positive organisms, including *Bacillus mycoides* and *Bacillus cereus*, and against gram-negative organisms, including *Pseudomonas fluorescens*, *Pseudomonas aeroginosa* and *Serratia marcescens*, while its toxicity for animals is sufficiently low that it has therapeutic interest for diseases such as tularemia,[2] typhoid fever,[3] tuberculosis[4] and brucellosis.[5] Streptothricin[6] was obtained first in 1942 as a crude concentrate which was prepared from cultures of *Streptomyces lavendulae*. It is also active against gram-negative organisms, including the three mentioned above, but is relatively much less active[1] against such gram-positive organisms as *Bacillus mycoides* and *Bacillus cereus*. Streptothricin also appears to have possible therapeutic applicability.[7]

The concentrates of streptomycin and streptothricin which were used for these biological studies[1, 6] were prepared by adsorption of the active substance from the culture medium by means of Norite-A, elution of the active substance from the adsorbate with dilute acid, neutralization of the eluate and concentration *in vacuo* to a residue. A concentrate of streptothricin was made also by eluting the adsorbate with acidified alcohol, neutralizing the eluate and adding ether to the eluate.[8]

We have studied methods for the purification and isolation of these active substances and have found that when rather highly purified concentrates of streptomycin were treated with methyl orange (the sodium salt of helianthine) a crystalline salt formed which served for purification of the active principle. This helianthate can be converted into the hydrochloride, sulfate or any other suitable salt for chemical or therapeutic purposes. Concentrates of streptomycin hydrochloride were treated with methyl orange and by metathetical reaction yielded the insoluble crystalline streptomycin helianthate. Since this salt is relatively insoluble in water, it separates satisfactorily from an aqueous methanol solution and was recrystallized from the same solvent. Solvent of crys-

[4] We are indebted to Dr. Wickerham of the NRRL, Peoria, for the culture of *S. globosus*.

[1] A. Schatz, E. Bugie and S. A. Waksman, *Proc. Soc. Exp. Biol. and Med.*, 55: 66, 1944.

[2] F. R. Heilman, *Staff Meetings of Mayo Clinic*, 19: 553, 1944.

[3] H. J. Robinson, D. G. Smith and O. E. Graessle, *Proc. Soc. Exp. Biol. and Med.*, 57: 226, 1944; H. A. Reimann, W. F. Elias and A. H. Price, *Jour. Am. Med. Asn.*, 128: 175, 1945.

[4] W. H. Feldman and H. C. Hinshaw, *Staff Meetings of the Mayo Clinic*, 19: 593, 1944; A. Schatz and S. A. Waksman, *ibid.*, 57: 244, 1944.

[5] D. Jones, H. J. Metzger, A. Schatz and S. A. Waksman, SCIENCE, 100: 103, 1944.

[6] S. A. Waksman and H. B. Woodruff, *Proc. Soc. Exp. Biol. and Med.*, 49: 207, 1942.

[7] H. J. Metzger, S. A. Waksman and L. H. Pugh, *Proc. Soc. Exp. Biol. and Med.*, 51: 251, 1942; H. J. Robinson, O. E. Graessle and D. G. Smith, SCIENCE, 99: 540, 1944; H. J. Robinson and D. G. Smith, *Jour. Pharm. and Exp. Therap.*, 81: 390, 1944.

[8] S. A. Waksman, *Jour. Bact.*, 46: 299, 1943.

tallization was present, but after heating at 100° *in vacuo* the anhydrous form was obtained. This anhydrous product darkened at 205° and melted with decomposition at 220–226° (micro-block).

Assays were carried out by Dr. H. B. Woodruff and Mr. D. Hendlin, of the Microbiological Department. Employing *B. subtilis* as a test organism in a cup assay method which they developed, they found an activity of about 350 units/mg for streptomycin helianthate. The various other salts described in this paper were assayed in the same manner.

The results of some microanalytical determinations on the dried streptomycin helianthate follow: Found: C, 50.38, 50.29; H, 5.86, 5.56; N, 14.48, 14.64; S, 5.76.

Streptomycin helianthate was converted to the hydrochloride by treating the salt with a mixture of methyl alcohol and hydrochloric acid. The liberated helianthine was removed and the hydrochloride was precipitated with ether from the filtrate. The hydrochloride was obtained as a white powder. When dried at 25° *in vacuo* over phosphorus pentoxide, streptomycin hydrochloride showed a specific rotation $(\alpha)_D = -84°$ (C, 0.5 per cent. in water), and an activity of about 800 units/mg. The results of microanalytical determinations on a sample dried at 100° *in vacuo* follow: Found: C, 36.60, 36.42; H, 6.04, 6.20; N, 13.42; Cl, 14.80; ash, none. Tests for the presence of sulfur and phosphorus gave negative results. The ultraviolet adsorption spectra of streptomycin in phosphate buffer at pH 7, in glycine buffer at pH 2 and in borate buffer at pH 9 showed only end absorption below about 2,300 Å.

The above analytical data alone are not sufficient for establishing firmly the true empirical formulae of streptomycin, its hydrochloride and its helianthate. These results need to be interpreted in conjunction with molecular weight determinations and other information. Furthermore, the possible molecular weight of about 700 for streptomycin hydrochloride adds to the difficulties of exact determination of empirical formulae. After more complete data are obtained, the results will be presented in detail.

The crystalline salt of streptomycin and *p*-(2-hydroxy-l-naphthylazo)-benzenesulfonic acid was prepared from streptomycin hydrochloride and Orange II. This salt showed an activity of about 300 units/mg. The preparations of streptomycin sulfate, which have been obtained crystalline, have shown about 520 units/mg.

Streptothricin helianthate was prepared using the same method. The crystals melted with decomposition at 220–225° (micro-block) and had an activity of about 400 units/mg.

The authors wish to acknowledge the cooperation of Messrs. C. E. Hoffhine, Jr., R. P. Graber and E. Flynn on the isolation work, and of Dr. N. R. Trenner and Mrs. F. A. Bacher for the absorption spectra determinations.

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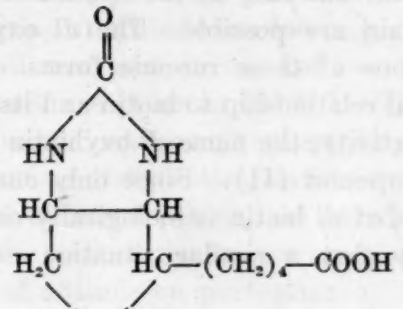
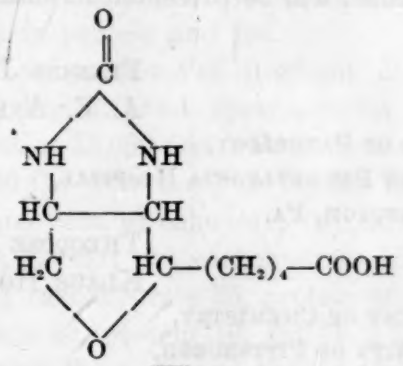
THE MICROBIOLOGICAL ACTIVITY OF AN OXYGEN ANALOG OF BIOTIN

THE synthesis of a *dl*-hexahydro-2-oxo-l-furo [3, 4] imidazole-4-valeric acid, an oxygen analog of biotin, has been recently described.[1] The structural relationship between biotin (I) and this new compound (II) is indicated by the following formulae.



(I)



(II)

The growth-stimulating activity of the oxygen analog under conditions in which biotin is the limiting factor has now been determined for three microorganisms: *Lactobacillus arabinosus*,[2] *Lactobacillus casei*[3] and *Saccharomyces cerevisiae*.[4] The methods were, with slight modifications, those described in the literature cited.

On a weight basis, the *dl* oxygen analog is one half as active as natural *d* biotin when assayed with *L. arabinosus*. Its activity for *L. casei* is slightly lower, approximately 40 per cent. that of *d* biotin. With

[1] K. Hofmann, *Jour. Am. Chem. Soc.*, 67: 694, 1945.
[2] L. D. Wright and H. R. Skeggs, *Proc. Soc. Exp. Biol. and Med.*, 56: 95, 1944.
[3] M. Landy and D. M. Dicken, *Jour. Lab. and Clin. Med.*, 27: 1086, 1942.
[4] R. Hertz, *Proc. Soc. Exp. Biol. and Med.*, 52: 15, 1943.

each of these microorganisms the shapes of the growth curves are identical for the two compounds and the same growth maxima are attained.

However, with *S. cerevisiae* the growth curve of the oxygen analog differs somewhat from that of biotin. Different activity ratios at various portions of the curves are, therefore, obtained. Thus, at one-half maximum growth, the activity of the *dl* oxygen analog is 25 per cent, that of *d* biotin, whereas at maximum growth this compound is only 8 per cent as active. The same growth maximum is obtained with both compounds. Whether the oxygen analog is active as such or exerts activity because of its transformation into biotin remains to be elucidated.

The procedures employed in the synthesis of the oxygen analog have demonstrated the *cis* configuration of the two fused rings. Therefore, only two racemic forms differing in the spatial orientation of the side chain are possible. The *dl* oxygen analog represents one of these racemic forms. Because of its structural relationship to biotin and its comparable biological activity, the name *dl*-oxybiotin is proposed for this compound (II). Since only one of the enantiomorphs of *dl* biotin is biologically active,[5] it appears likely that a similar situation exists for *dl* oxybiotin.

Studies now in progress on the activity of oxybiotin and related compounds, both for animals and for microorganisms, will be presented in subsequent publications.

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OBSERVATIONS ON THE EFFECT OF PREFLIGHT MEALS UPON ALTITUDE TOLERANCE[1]

ALTITUDE tolerance represents only one aspect of preflight and inflight feeding of aviation personnel, but under many circumstances it represents an important consideration. Both empirical observations and carefully controlled experiments indicate the need for food intake at approximately normal meal-time intervals, in order to maintain optimal performance. Hence timing and attractiveness are important aspects of aviation feeding, in addition to provision for an optimal state of nutrition in terms of general health and the maintenance of optimal performance capacity during special stress periods.

The high protein foods, such as meat, milk, eggs and cheese should be consumed in generous quantities, from a long-time point of view, to provide proteins of high quality, minerals and vitamins, and to maintain good morale.

From the point of view of altitude tolerance, however, meals relatively high in carbohydrate afford a distinct advantage when consumed during flight or at the meal preceding altitude exposure. References to the literature and a more detailed discussion of the physiological background of this relationship have been given in an earlier publication,[2] together with experimental data illustrating the gain in altitude tolerance afforded by meals having a relatively high carbohydrate content. Among the factors that apparently contribute to better altitude tolerance after high carbohydrate meals are (a) lesser oxygen demand, (b) higher carbon dioxide production rate, (c) maintenance of glycogen reserves and (d) lessened impairment from alkalosis. In order to achieve the optimum benefits from a high carbohydrate intake, a fairly high caloric intake is necessary, and there is some indication of a slight additional gain from a normal fluid intake.

Not uncommonly a question arises regarding the risk of inter-meal hypoglycemia subsequent to high carbohydrate meals, as a possible factor that might offset the advantages gained during short exposure periods. In the tests performed thus far, however, there has been no evidence of an appreciable risk of that nature when the caloric intake has been adequate.

Because unnecessary impairment is apt to occur after an interval of 6 to 7 hours or less, irrespective of the nature of the preceding meal, there is good reason to provide a convenient reserve or emergency source of food for consumption by flight personnel when unexpected extensions of flight time are encountered.

EXPERIMENTAL

Visual Field: A section of the upper right quadrant of the visual field of the right eye is plotted for sensitivity to a 0.4 mm white test object against a dark ground. The technique was adapted from Evans's procedure for plotting "angioscotoma," using a Lloyd stereocampimeter. The recorded figure is the area of campimeter surface (square inches) within which the object is not seen.

[5] J. L. Stokes and M. Gunness, *Jour. Biol. Chem.*, 157: 121, 1945.

[1] The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development (Contract OEMcmr–224) and Columbia University, and with the aid of a grant from the Nutrition Foundation.

[2] C. G. King, Hylan A. Bickerman, Winifred Bouvet, C. J. Harrer, James R. Oyler and C. P. Seitz, *Jour. Aviation Medicine* (1945, 16: 69).

Block test: The subject's task is to place 60 cylindrical wooden blocks, 1.5 inches in diameter, into a simple pattern of holes in a board placed at a convenient height. The score is the average time (seconds) on four successive trials.

Pursuitmeter: In this test the subject observes and adjusts to alignment a horizontal white bar which is moved up and down irregularly by a hidden mechanism. The task is to compensate for the movement imposed by the mechanism, by forward or backward movement of a "stick" held in both hands by the subject. An electric clock records the total amount of time, within a two-minute trial, that the bar is kept centered between two guide lines.

Addition test: A test of mental arithmetic consisting of fifty addition problems, in which the score is the number of correct solutions within a 3 (or 2½) minute interval. Equivalent forms are used for the different trials on a given day.

Self-rating: Each subject rates himself on 10 aspects of feeling and attitude. Rating is indicated for each variable by a mark on a base line, and the score is the average distance (in mm) of the ten marks from the unfavorable end of the scale.

Experimenter's rating: Each subject is rated by the same experimenter on 10 aspects of appearance and behavior, using a numerical scale from 1 to 10. The score is the average of the ten ratings.

All subjects were given preliminary practice on the block test, pursuitmeter and addition test sufficient to carry them well beyond the initial phase of rapid learning.

TABLE 1

EFFECTS OF ANOXIA ON PERFORMANCE AND RATING IN RELATION TO THE COMPOSITION OF THE PREFLIGHT MEAL*

Type of luncheon	Visual field Per cent.	Block test Per cent.	Addition test Per cent.	Self-rating Scale units	Experimenter's rating Scale units
Protein	12.1	24.2	16.1	2.6	5.1
Carbohydrate	3.7	10.7	8.9	1.0	4.6
Difference ..	8.4	13.5	7.2	1.6	.5
Reliability† .	96	99	77	98	96

* Tests started 1–¾ hours after lunch and ½ hour after reaching a simulated altitude of 17,000 feet. Testing continued for 2 hours. Values for 8 subjects are based upon impairment relative to ground level, except in case of experimenter's rating.

† Chances in 100 that the difference is real.

Test scores and self-ratings were obtained once each day at ground level, and two or more times at altitude. Results are reported in terms of impairment or difference between ground level and altitude score. The experimenter's rating was ordinarily recorded at altitude only; hence the ratings gave an index of absolute condition measured in scale units rather than a direct measure of impairment.

Data from a typical series of tests are given in Table 1. Eight subjects were exposed at 17,000 feet on each of four afternoons, beginning about 1¾ hours after a 1,000 calorie lunch. The percentage composition on a calorie basis, of the meals served on Monday and Friday, was: carbohydrate 92, protein 5, fat 3; and of the preflight meals served on Tuesday and Thursday: carbohydrate 12, protein 47, fat 41. Lunch was eaten between 12:00 and 12:30; ground level testing was between 1:00 and 2:00; and altitude was reached at approximately 2:15. Two successive series of tests were conducted during each run, starting one-half hour after reaching altitude and continuing over a period of two hours. The addition test was done once, at the end of the first series, about one hour after ascent; the experimenter's rating was done once, at the end of the second series of tests. Scores for two tests of visual field, block test and self-rating at altitude were averaged, and average data for all measures during the two days on each type of lunch are given in Table 1. This procedure makes the individual the unit of sampling in the statistical treatment. Reliabilities, stated as chances in 100 that a real difference exists, are satisfactorily high, especially in view of the known random variation in the effect of altitude on performance. The data are typical of results obtained during two and a half years of testing, in that preflight meals relatively high in carbohydrate afford better altitude tolerance than meals high in protein and fat.

Further comparisons of preflight diets are summarized in Fig. 1, based upon a series of tests with five subjects at 15,000 feet. Four diets of equicaloric value (1000 C.) were used, having the following composition (per cent. of calories): (a) carbohydrate 70, protein 10, fat 20; (b) carbohydrate 55, protein 20, fat 25; (c) carbohydrate 25, protein 40, fat 35; (d) carbohydrate 20, protein 10, fat 70. The technique of conducting the tests and the schedule of feeding and exposure were essentially as outlined above. The results are typically favorable toward high carbohydrate preflight meals, except that the gain observed in the visual testing was less than has been observed frequently.

Because of the well-known tendency of foods high in protein and fat content to digest more slowly than foods high in available carbohydrate and their tendency to result in lesser fluctuation in blood sugar concentration, there was an obvious need to consider whether 1,000 calorie meals relatively low in protein and fat content would result in lowered efficiency of performance within a normal between-meal interval. Tests were conducted therefore through a longer interval than studied in detail previously, at an altitude of 15,000 feet, and including measurements at four

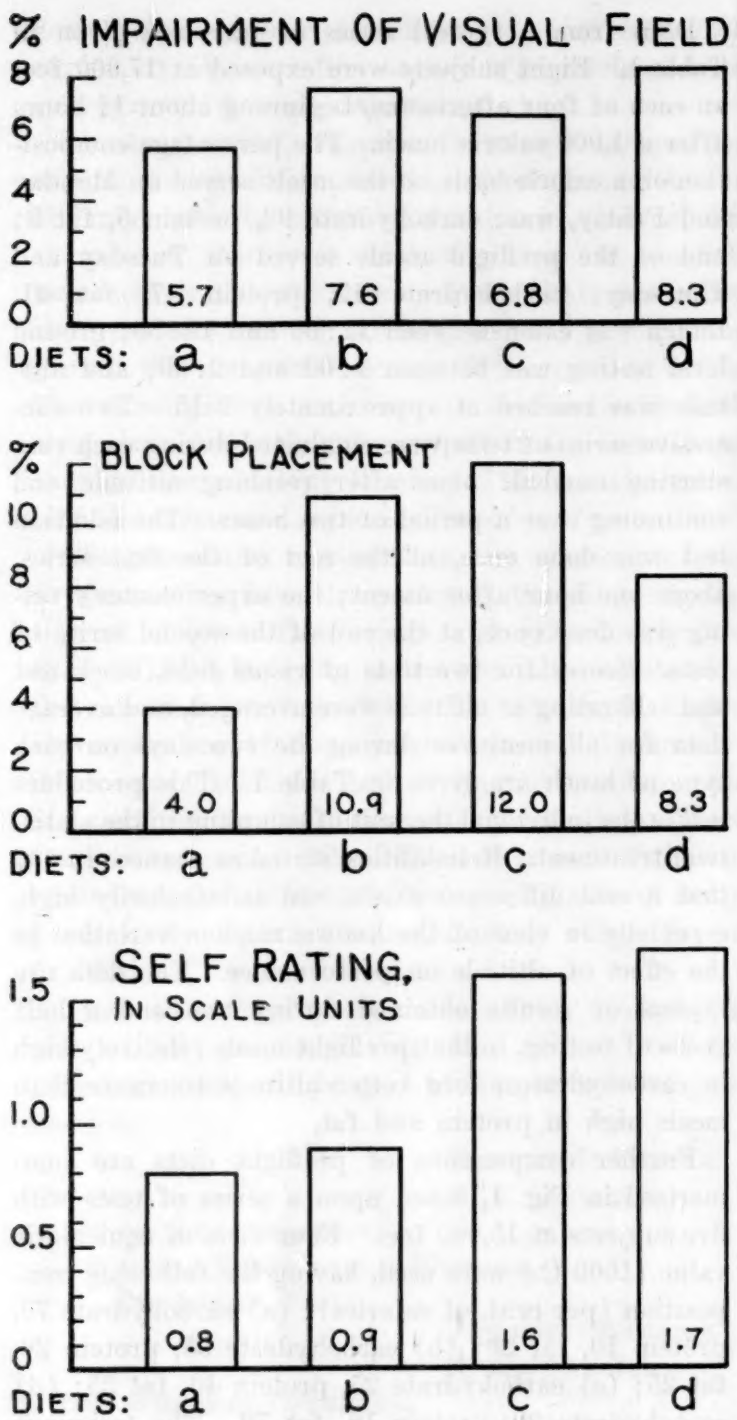

FIG. 1. Impairment during 2 hr. exposure of five subjects at 15,000 ft. Height of column in each case represents degree of impairment. Composition of test meals, in per cent. of total (1000) calories: *a*, carbohydrate 70, protein 10, fat 20; *b*, carbohydrate 55, protein 20, fat 25; *c*, carbohydrate 25, protein 40, fat 35; *d*, carbohydrate 20, protein 10, fat 70.

intervals, the last set beginning at 6 hours after lunch and ending within the ensuing hour.

Eight subjects were divided into two equal groups and exposed on four different days. On each of the experimental days one group consumed a high carbohydrate lunch (carbohydrate 92, protein 6, fat 2) and another group received an equicaloric (total—1,000 C.) low carbohydrate lunch (carbohydrate 21, protein 43, fat 36). By reversing the groups on two of the days, more consistent data were obtained than when the entire squad was given the same type of lunch.

The high carbohydrate meals held their advantage for approximately 6 hours, covering the normal interval between successive meals. Some of the tests showed slightly more and others less impairment during the 6- to 7-hour period of testing, in comparing the two types of meals, but none of the eight subjects showed a distinct tendency toward impairment as a result of the preceding meal being low in protein and fat. The average results from tests of visual field, block placement, pursuitmeter, addition, self-rating and experimenter's rating were nearly equal for the two test meals at the last period of testing.

It has been our experience and it has been demonstrated in tests conducted by the armed services that it is practical, when maximal altitude tolerance is desired, to provide attractive and satisfactory meals from regular food supplies, such as the "B" ration, having a protein content in the range of 8 to 12 per cent. of the total calories.

Preflight and inflight meals relatively high in carbohydrates, which afford increased altitude tolerance, can be followed by meals correspondingly high in protein, to provide an over-all food intake of high nutritive quality and excellent acceptability.

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STUDIES IN MECHANISMS OF PENICILLIN ACTION. I. PENICILLIN EFFECTS ON BLOOD COAGULATION

IN the course of studies on the blood levels attainable with varying dosages of penicillin given both by the oral[1] and intra-muscular routes, it was ob-

[1] L. F. Moldavsky and Wm. B. Hesselbrock, "Oral Penicillin" (in press).

served that within minutes after administration of the drug there was a marked increase in the speed with which the blood clotted. In some instances so marked was this phenomenon that coagulation occurred in the syringe before the blood could be expelled. This finding, together with the known tendency towards thrombosis when penicillin is given intravenously, led us to measure this phenomenon more quantitatively by the simple laboratory determinations of the clotting and bleeding time.

The data obtained so completely affirmed this incidental observation that, although these studies are in their early phase, a preliminary note seemed justifiable.

As part of the analysis of this effect prothrombin time determinations have already been begun and serum calcium studies are planned.

EXPERIMENTAL DATA

In 20 patients to whom both oral penicillin (enteric coated capsules—each containing 100,000 units) and intra-muscular penicillin were given, the concentration of penicillin in the blood, at the same time the clotting time, bleeding time and prothrombin time, was measured. The determinations were made before penicillin was given, than at 15- and 30-minute intervals after its administration. The experiments were begun each morning and food and water withheld to maintain uniform conditions for the duration of the experiment. Determinations of clotting time, bleeding time and prothrombin time were also carried out in a group of controls under the same conditions.

Clotting time was determined both by the use of the capillary tube and by the method of Lee and White. Duke's method for bleeding time and Howell's method for prothrombin time determination were utilized for the data obtained concerning these variables. It is recognized that Howell's method for prothrombin time estimation is of limited value and no attempt is made to draw any conclusions from these determinations. It is planned to repeat these prothrombin determinations by the use of more accurate laboratory methods.

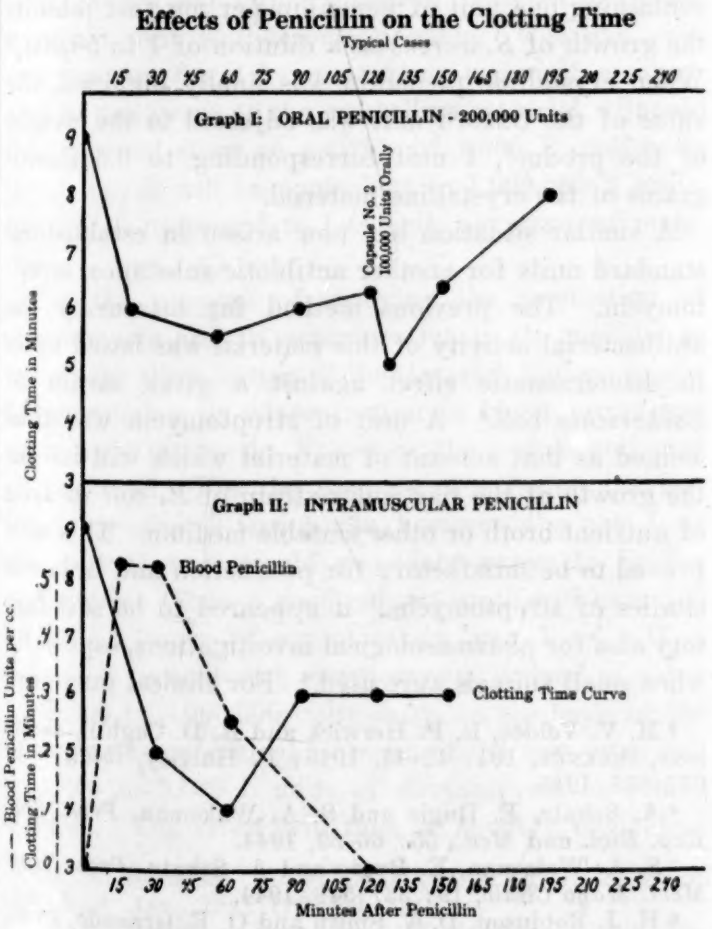
RESULTS

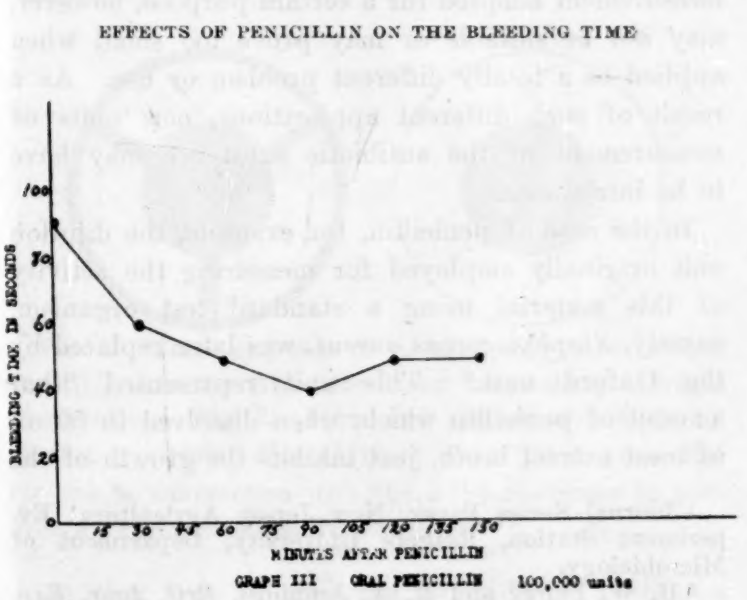
The absence of change in the clotting time exhibited by the control group sharply contrasted with the sharp fall shown when oral penicillin (Graph I) or intra-muscular penicillin (Graph II and Table 1) was given. It was found (Graph II) that as the concentration of penicillin in the blood rose, the clotting time fell, and persisted at a depressed level even after penicillin had completely disappeared from the

TABLE 1

EFFECT OF PENICILLIN (INTRAMUSCULAR) ON CLOTTING TIME; A TYPICAL CASE

	Capillary-tube method	Test-tube method
Control	4 min. 30 sec.	17 min.
PENICILLIN—50,000 UNITS INTRAMUSCULARLY		
After 10 minutes	2 min. 40 sec.	8 min.
After 25 "	1 " 30 "	6 " 30 sec.
After 40 "	1 " 50 "	6 " 20 "
After 1 hour	2 " 40 "	6 " (slightly less)
After 1 hour 40 min.	2 "	6 "
After 2 hours	1 " 55 "	6 "
After 3 "	1 " 30 "	7 " 10 sec.




EFFECTS OF PENICILLIN ON THE BLEEDING TIME
BLEEDING TIME IN SECONDS
MINUTES AFTER PENICILLIN
GRAPH III ORAL PENICILLIN 100,000 units

blood. In several of the experiments this depression persisted for as long as an hour after penicillin had been completely excreted from the blood, on others there was a more rapid return to the control value for that particular patient.

The bleeding time, which in the control group also remained constant, fell when penicillin was given (Graph III). The curve of descent was not quite so marked, and from these early results seemed more transient.

The prothrombin times have so far not shown a characteristic uni-directional change.

Discussion

This consistent, penicillin-evoked alteration of the blood possesses two components. The first one, the hastening of the coagulation of the blood, has already been described. The second is an even more startling change in the nature of the clot itself. There is produced, as a result of the increased penicillin level in the blood, a non-retractile clot; the blood is dark and exceedingly viscous in its flow, and when coagulation is complete it appears solidified. The appearance of the coagulated blood is that of an artificially produced solid thrombus. The mechanism of this peculiar clotting response is deserving of complete analysis, and such studies are planned.

There is a twofold clinical significance to be attached to these findings. First, they serve to emphasize the danger of thrombus formation with penicillin administration. This becomes more important with the newer tendency to increase dosages employed to augment clinical effect. Second, they suggest investigative studies to test the value of the drug as a coagulant in hemorrhagic disorders.

The authors wish to acknowledge their appreciation for the cooperation and encouragement given to them by Col. G. V. Emerson, Commanding Officer of the Harmon General Hospital, and Lt. Col. William 0. Johnson, Chief of the Surgical Service.

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Captain, SnC.
Carlos Cateno,
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SCIENTIFIC APPARATUS AND LABORATORY METHODS

STANDARDIZATION OF STREPTOMYCIN[1]

In the isolation and purification of antibiotic substances, the bacteriologist has to depend upon biological assays. Until the chemical nature of the active agent has been established and until a suitable chemical test has been developed, the chemist, as well, has to depend upon such methods. This is true also of the pharmacologist and of the clinician, who study the effectiveness of such materials *in vivo*. The unit of measurement adopted for a certain purpose, however, may not be suitable or may prove too small when applied to a totally different problem or use. As a result of such different applications, new units of measurement of the antibiotic substance may have to be introduced.

In the case of penicillin, for example, the dilution unit originally employed for measuring the activity of this material using a standard test organism, namely, *Staphylococcus aureus,* was later replaced by the Oxford unit.[2] This unit represented "that amount of penicillin which, when dissolved in 50 ml of meat extract broth, just inhibits the growth of the test strain of *Staphylococcus aureus*. Thus material containing one unit of penicillin per mg just inhibits the growth of *S. aureus* at a dilution of 1 to 50,000." When crystalline penicillin was finally obtained, the value of the Oxford unit was adjusted to the weight of the product, 1 unit corresponding to 0.6 micrograms of the crystalline material.[3]

A similar situation has now arisen in establishing standard units for another antibiotic substance, streptomycin. The previous method for measuring the antibacterial activity of this material was based upon its bacteriostatic effect against a given strain of *Escherichia coli*.[4] A unit of streptomycin was thus defined as that amount of material which will inhibit the growth of the particular strain of *E. coli* in 1 ml of nutrient broth or other suitable medium. This unit proved to be satisfactory for production and isolation studies of streptomycin;[5] it appeared to be satisfactory also for pharmacological investigations, especially when small animals were used.[6] For clinical purposes,

[1] Journal Series Paper, New Jersey Agricultural Experiment Station, Rutgers University, Department of Microbiology.

[2] H. W. Florey and M. A. Jennings, *Brit. Jour. Exp. Path.*, 23: 120–123, 1942.

[3] M. V. Veldee, R. P. Herwick and R. D. Coghill, *chairman,* Science, 101: 42–43, 1945; P. Hartley, *ibid.*, 101: 637–638, 1945.

[4] A. Schatz, E. Bugie and S. A. Waksman, *Proc. Soc. Exp. Biol. and Med.*, 55: 66–69, 1944.

[5] S. A. Waksman, E. Bugie and A. Schatz, *Proc. Staff Meet. Mayo Clinic,* 19: 537–548, 1944.

[6] H. J. Robinson, D. G. Smith and O. E. Graessle, *Proc. Soc. Exp. Biol. and Med.*, 57: 226–231, 1944.

however, too many units are required,[7] thus giving the impression that large doses of the material are needed for effective chemotherapeutic purposes.

The problem of defining a streptomycin unit becomes especially complicated when attempts are made to compare the *in vivo* activity of streptomycin with that of penicillin, especially when the measurement of the latter is based on the Oxford unit.[8] The fact that the basis for the standardization of the two materials is different, and, further, the use of two different test organisms can only lead to much confusion. This becomes clear when one compares the above figures given for the Oxford unit with the unit of streptomycin which is based upon inhibition of growth in 1 ml of medium; the Oxford unit is thus found to represent a far greater *in vitro* activity than the streptomycin unit.

Because of these considerations, it is proposed here to establish the following three units for designating streptomycin:

(1) An S unit, or that amount of material which will inhibit the growth of a standard strain of *E. coli* in 1 ml of nutrient broth or other suitable medium. This unit will thus correspond to the original *E. coli* unit.

(2) An L unit, or that amount of material which will inhibit the growth of a standard strain of *E. coli* in 1 liter of medium. An L unit is thus equivalent to 1,000 S units.

(3) When crystalline material becomes available, a weight unit will become possible. One can even now prepare for it by recognizing a G unit, comparable to one gram of the crystalline material. Should this material show an activity of 1,000 *E. coli* units per 1 mg, it will be equivalent to 1,000,000 S units, to 1,000 L units and to 1 G unit, per gram of material.

For the purpose of studying the production of streptomycin and its concentration in the medium as well as for the isolation of the material, and especially for measuring its concentration in blood, urine and other body fluids, the *E. coli* or the new S unit may still be used. For the purpose of utilizing the material for clinical treatments, however, the new L or even the G unit would no doubt prove to be far preferable. Thus, a good culture broth will have 100 to 200 S units of streptomycin per 1 ml. If a patient is treated with streptomycin, instead of using 1,000,000 to 5,000,000 units daily, on the basis of the old unit, the equivalent in terms of the new units will be 1,000 to 5,000 L units of streptomycin or 1 to 5 G units. The latter will thus be roughly equivalent to about 5 gm of the purified material. The concentration of streptomycin in the blood of the patient may be 0.5 to 50 S units, depending on dosage used and rate of excretion.

The units of measurement of streptomycin are thus based upon the inhibition of growth of a standard strain of *E. coli*, as determined by the dilution method, using either a series of dilutions in liquid media or the agar plate streak method. The actual determinations are carried out by the agar diffusion or so-called cup method, using either a standard strain of *Bacillus subtilis* or *S. aureus*. Other convenient procedures, such as the turbidimetric method, can also be employed. A given preparation of streptomycin, preferably the crystalline product when it becomes available, is used as a standard for determining the potency of unknown lots of broth or of the isolated product.

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[7] H. A. Reimann, W. F. Elias and A. H. Price, *Jour. Am. Med. Asn.*, 128: 175–180, 1945.

[8] F. R. Heilman, *Proc. Staff Meet. Mayo Clinic*, 20: 169–176, 1945.

DARKFIELD ILLUMINATORS IN MICROSCOPY

IT is usually recommended that a microscope be equipped with a special darkfield condenser and a funnel stop solely for darkfield work. An improvised darkfield stop has been found to be a satisfactory substitute for the darkfield condenser in the experience of the writer.

A special stop is generally supplied with the microscope by the manufacturer. An improvised darkfield stop can be made by having a piece of thin metal cut in the form shown in the illustration (Fig. 1), and of such a size that the outer narrowing ring fits snugly into the slot provided in most substage Abbe condensers.

FIG. 1. Form and size of metallic stop used in conjunction with the Abbe condenser to produce darkfield illumination. Fig. 2. Form and size of stop made by pasting a circular disc of black paper on a glass disc for use in conjunction with the Abbe condenser to produce darkfield illumination.

Another type of stop can be made by pasting a circular disc of black paper in the center of a large

round cover glass or on the glas disc which is generally furnished with the microscope (Fig. 2).

A little experimentation will indicate the proper size of the central disc, which depends upon the aperture of the objective used. The relation of condenser, specimen and objective is the same as with the regular darkfield illuminator: $Limit\ of\ Resolution = \frac{0.5\,\lambda}{N.A.}$ *where* λ *is the wave-length of light used and N.A. is the numerical aperture of the objective.*

A satisfactory examination under oil immersion can be made if a funnel stop is inserted in the objective to reduce the aperture of the oil immersion lens.

The use of improvised darkfield illumination has the advantage of allowing a rapid shift from the light to the dark field without disturbing the relation of the objective, specimen or condenser. Results with this apparatus may be relied upon for the demonstration of Treponema.

Directions for Use of Improvised Darkfield Illumination

Insert the stop in the special ring beneath the Abbe condenser. Lower the substage and place a drop of immersion oil, free of bubbles, on the upper surface of the condenser. Put the slide preparation on the stage and center the specimen. Raise the substage until the oil is spread by contact with the slide, filling the space between the slide and condenser. Examine under low and high power. If examination under oil immersion is desired, it may be accomplished by properly inserting a funnel stop in the oil immersion objective and placing a drop of immersion oil on the coverslip before lowering the objective over the specimen. It is important that a strong light source be employed.

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Board of Health,
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DISCUSSION

AN APPROACH TO THE NUTRITION PROBLEMS OF OTHER NATIONS

During the past several years, the Nutritional Biochemistry Laboratories of the Massachusetts Institute of Technology, in collaboration with the Mexican Institute of Nutrition and the Pan American Sanitary Bureau, have been working in the training of food chemists and nutritional clinicians; in the analysis of Mexican foods[1]; in the appraisal of the nutritional status of Mexican school children; and in the development of a school lunch program in Mexico City. As a result of this experience several observations have been made as to what appear to be the most practical approaches to the solution of the food and nutrition problems of countries other than our own. While it is realized that more extensive experience may modify some of these observations, they are presented at this time for the guidance of those actively concerned with the food problems of other countries, especially those in Latin America. No attempt is made to discuss here the adequacy or inadequacy of food production in the United States to meet the needs of other nations. The current controversy on that subject only serves to emphasize the desirability of examining carefully every practical approach to the problem of feeding mankind.

Nutritive Quality of Foods

Because of the high nutritive quality of indigenous Mexican foods it was not difficult to formulate a school lunch containing one third of the daily allowance[2] of protein, calories, minerals and vitamins. Most Mexican foods are unknown in the United States; similarly many American foods are not widely consumed in Mexico. For instance, milk, meat and eggs, while admittedly excellent foods, can not be used extensively there because of high cost, low production and inadequate transportation.

In our investigations, we have encountered several very nutritious food plants which are eaten by significant segments of the Mexican population. One of these is malva, an uncultivated plant which grows extensively on the Mexican plateau. Its leaves are eaten much as we eat spinach. A serving of malva (100 grams) can supply 40 per cent. of the calcium, 90 per cent. of the iron, 140 per cent. of the vitamin A (as carotene), 60 per cent. of the ascorbic acid and a significant portion of the thiamine and niacin allowances[2] for adult man. Charal, sesame seed, calabaza seed, pulque, piñón and corn tortilla are foods especially rich in various nutrients.

Nutritional Status of People

The effect of the high nutritive value of Mexican foods was reflected in the nutritional status of the people. Malnutrition appeared to be no more common[3] among a group of 1,000 children in a poverty-stricken area of Mexico City than in a group of 800 children from middle-class families in Michigan.[4]

[1] R. Cravito, E. E. Lockhart, R. K. Anderson, F. de P. Miranda and R. S. Harris, *Jour. Nutrition*, 29: 317, 1945.

[2] "Recommended Dietary Allowances," Reprint and Circular Series No. 115, National Research Council, 1943.

[3] E. E. Lockhart, *et al.*, unpublished data.

[4] R. S. Harris, E. Weeks and M. Kinde, *Jour. Am. Diet. Assoc.*, 19: 182, 1943.

A study has been made of the foods eaten by Indians living in the Mesquital valley some 80 miles from Mexico City. This valley is so arid and desolate as to cause one to wonder how there is sufficient vegetation to feed the numerous villages which spot the area. Yet these native tribes have survived through the centuries upon foods gleaned from this forbidding soil and show surprisingly little evidence[5] of malnourishment. The problem in such areas is not one of malnutrition but of undernutrition. Though the quality of the diet is satisfactory, the quantity may be below that necessary for best growth and development.

Food Habits

Food habits seem to be highly developed in areas such as the Mesquital. Each food habit that we have investigated has been found to have a scientific justification. Thus, the lime which is used in the treatment of corn during the preparation of tortillas contributes a very significant quantity of calcium to a people whose diets are otherwise calcium-deficient.

Hot chili is surprisingly rich in carotene and as little as 6 grams of some varieties will furnish the entire daily allowance[2] of vitamin A. It is interesting that chili is deep-seated in the food habits of a population whose diets are low in vitamin A content. Food habits may not always be based on nutritional needs, yet the traditional food habits of a people who have survived successfully in an adverse food environment must necessarily embody choices of great nutritional significance which were probably made blindly or through uncritical trial and error. In such areas the analysis of edible plants can identify now those particular foods which a population might eventually find in its groping for a better diet during centuries to come. Thus, the progress of a people toward an improved utilization of better indigenous foods can actually be hastened.

Because food habits often have a scientific justification, they should not be altered until one is certain that the substituted food will supply the quantities of all nutrients formerly provided. Even then it may not be advisable to encourage changes until data are available as to their effect upon such things as the synthesis of vitamins by intestinal bacteria. The habits of peoples with long-established food cultures should be regarded as inviolable until they have been most carefully analyzed.

There is a danger in forcing dietary changes on other countries. Our sense of preference and superiority and their inordinate respect for our prestige position tempts us to believe that ours is the preferred way of living. Thus, we may be deluded into believing that good nourishment can not be achieved unless milk, meat, eggs and certain designated vegetables are a part of the daily dietary. Though this may be the American pattern of good nutrition, there are many parts of the world where this pattern should not be advocated. The foodstuffs which most effectively and economically assure good nutrition in the United States are not those which can best nourish the people of Mexico or China or elsewhere. Good nutrition consists in supplying all nutrients in the amounts necessary for the best growth, development and maintenance of all body tissues. The particular foodstuffs which serve as sources of these nutrients are themselves of no particular importance. Calcium is nutritious whether it comes from milk or Mexican tortilla.

Nutrition education in any given country should be patterned around the food habits of the people and formulated on the composition of native edible plant and animal products. It should not be based on the food pattern of any other nation. We have noted that a school lunch based on United States food habits costs approximately five times as much in Mexico City as a more nutritious school lunch based on Mexican food habits and foods.

Food Analysis

Exact analysis of all edible plants for all important nutrients is basic to the sound food and nutrition program of any country. Agricultural policy should be formulated only after all edible plants native to the area have been analyzed for nutrient content. Preference should then be shown for those crops which give the greatest yields with the most nutrition at the lowest cost. Food analysis can also guide geneticists in the selection of the most nutritious strains and varieties of plants. Our preliminary studies[6] indicate that through corn breeding the niacin content of the Mexican dietary may be raised significantly.

Assistance from the United States

Other nations may best be helped by (a) training key nutritional biochemists, nutritional clinicians, nutritionists, agronomists, economic botanists and specialists in food habits; (b) by supplying equipment necessary for food and nutrition research; (c) by sending field personnel abroad, first to direct and later to advise in practical nutrition research programs; and (d) by giving scientific instead of financial assistance in years to come.

Other nations will fail to solve their nutrition problems if we in the United States are permitted to impose our foods and food habits upon them. These nations will succeed as they learn that their way to good nutriton need not be our way. We in the United

[5] R. K. Anderson, *et al.*, in press.

[6] P. Mangelsdorf and R. S. Harris, in press.

States will be most constructive when we learn that other nations need our knowledge and skills, not our foods and food habits.

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NATIONAL ARCHEOLOGICAL RESOURCES

RESOLUTION CONCERNING THE CONSERVATION OF NATIONAL ARCHEOLOGICAL RESOURCES IN THE RIVER VALLEYS OF THE UNITED STATES

1. WHEREAS: There are now under consideration plans for the establishment of river valley authorities, comparable to the Tennessee Valley Authority, as well as other flood control and reclamation projects, in several if not all of the major drainage systems of the United States.

2. WHEREAS: Eighty per cent. of all archeological remains in the United States are concentrated in approximately 2 per cent. of its area—namely, the banks of its great rivers and tributary streams—due to the fact that early man, like his modern successors, lived, hunted, farmed, built his temples and buried his dead along these fertile river margins.

3. WHEREAS: It is obvious, therefore, that the damming and flooding of considerable stretches of these river systems would irretrievably cover or destroy vast and important archeological deposits in all such areas.

4. WHEREAS: These archeological remains consist of prehistoric settlements, temple or other mounds, burial places and human cultural deposits accumulated during many thousands of otherwise unrecorded years. Only by careful, scientific excavation can such archeological remains provide their widely ramifying and extremely important historical, scientific, economic and artistic contributions concerning the earliest settlements of man in America, the history of the development of basic American agriculture, the incidence and range of human pathology native to America, as well as a wealth of material specimens and facts to be derived from them. Such contributions are not only scientifically and artistically valuable, but also of perpetual interest and educational value to the present-day citizens of the United States.

5. WHEREAS: The potential scientific, educational and cultural value of the archeological record still buried in the river banks of the United States represents an important asset belonging to the entire nation. It is, moreover, an utterly unique American historical record and such parts of it as are destroyed unrecorded can *never* be replaced. Three hundred years of effort may re-create a burned forest but once a part of the human prehistoric record is flooded or carelessly dug up and thus destroyed, prior to scientific study, it is lost forever.

6. WHEREAS: In those areas where it is deemed advisable to create river valley authorities or similar projects involving flooding and concurrent alterations, it is quite possible to attain reasonably adequate conservation and utilization of archeological resources at a cost representing a very small fraction of the total expenditures involved in such operations.

7. *Therefore, be it resolved.*

That there should be incorporated in the organic law creating or perpetuating any and all river valley authorities or similar projects involving the flooding or alteration of areas including Federal lands, river, harbor and all other areas subject to Federal control, as well as areas including sections of more than one state, now, and in the future, explicit provisions for adequate conservation of archeological resources; and, further, that the term "adequate conservation of archeological resources" be defined in correct legal terminology to include all the following items (a–e):

(a) Archeologists selected for such employment must meet the Civil Service Commission's requirements for such positions and have the approval of the Bureau of American Ethnology, Smithsonian Institution.

(b) Prior to such alterations or flooding, such archeologists must be provided adequate facilities and time for the complete archeological mapping and test-pitting or sampling of the area concerned.

(c) Prior to such alterations or flooding, adequate time and facilities must be made available to the archeologists for the complete excavation of selected key sites in the area. If coordinated with the early plans this will not hold up schedules.

(d) Laboratory facilities must be made available for the processing and study, as well as the preservation in perpetuity, of the excavated archeological materials.

(e) Provisions must be made for adequate publication and dissemination of the scientific and historical results thus attained.

The Committee on the Basic Needs of American Archeology of the National Research Council
Signed WM. DUNCAN STRONG,
Chairman of the Committee

The Planning Committee of the Society for American Archaelogy
Signed FREDERICK JOHNSON,
Chairman of the Committee

Committee for the Recovery of Archaeological Remains
Signed WILLIAM S. WEBB,
Chairman of the Committee

NON-PERMEABILITY OF THE LACTATING BOVINE MAMMARY GLAND TO PENICILLIN

AMONG other factors, the possibility of success in treating mastitis by the intravenous route obviously depends on the degree of permeability of the lactating

bovine mammary gland to the penicillin molecule in the blood stream. At least one attempt to treat chronic *S. agalactiae* mastitis by this route has been recorded as a failure.[1] The appearance of penicillin in various body fluids in man following intravenous injection has been reported, and in the bovine, a selective absorption of penicillin from the blood by an active mammary gland might conceivably remove the drug from the blood stream at a rate comparable to that of the kidney, necessitating more frequent doses to maintain a desired blood level. To test this hypothesis, the milk from a Jersey heifer, free of mastitis, was tested for penicillin activity following intravenous injections.

Penicillin Injections: In the first trial, 80,000 Oxford units of a calcium salt of penicillin in eight ml of 0.95 per cent. saline were introduced into the jugular vein. In a second trial, a total of 500,000 units were administered in two portions of 15 ml each about one minute apart. Prior to the injection the four quarters of the udder were milked out until only small intermittent streams were obtained.

Sampling: During the six-hour period following the injection the animal was milked for three to four minutes at intervals of a half-hour, and in the subsequent six-hour period at intervals of an hour. A final sample was obtained 24 hours after the injection. The samples were held at 4° C for less than two hours before portions were removed to the assay cups.

Testing: Preliminary observations indicated that the cup method of assay is adaptable to milk solutions of penicillin and that milk enhances the action of penicillin against the test organism, as measured by the zone size. This effect is probably attributable to the high buffer content of the milk. The cup method is of particular value in testing turbid and non-sterile solutions, and is reasonably critical to about 0.2 Oxford unit, a value within the range of accuracy required for the purpose of this study. The test organism employed was *S. aureus* H. Controls of buffered distilled water containing two units of penicillin gave satisfactory zones after 18 hours of incubation at 37° C.

Results: Penicillin activity was not observed in any of the milk samples obtained in the 24-hour period following the intravenous injection of 80,000 units in the first trial and 500,000 units in the second trial. The samples obtained during the first six-hour period in the second trial were pooled and the cream and skimmed milk tested separately for penicillin. No zones of inhibition were observed.

Our observations do not lend supporting evidence to the value of the intravenous method for the treatment of chronic bovine mastitis with penicillin, and indicate that the lactating bovine mammary gland does not serve as a major systemic exit for penicillin in the blood.

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[1] C. S. Bryan, R. E. Horwood and C. F. Huffman, *Veterinary Medicine*, 40: 87–89, 1945.

ROTATION OF ELECTROLYTE BETWEEN INSULATED POLES OF MAGNET

F. EHRENHAFT has described an experiment in which a drop of $FeCl_3$ rotates between the poles of a permanent magnet from which it is electrically and chemically insulated by a coat of Piceïn wax. I stated, at the meeting of the American Physical Society, on January 19, that I had seen this experiment and that the insulation did not break down under a potential difference of 220 volts. At that time, however, I had not been able to obtain the effect.

By reproducing exactly F. Ehrenhaft's experimental set-up, the rotations were obtained at the Sloane Physics Laboratory. The waxed pole faces were 1.5 mm apart. Light from a carbon arc was sharply focused on the center of the drop of $FeCl_3$ with the help of two lenses, the second of which was a microscope objective of focal length less than 2 cm. The drop was observed with a microscope. The insulation was checked electrically.

By observing the drop with the naked eye it was found that the motion was not a true rotation. The liquid moves both to the right and to the left, in a horizontal plane, and definite up and down motions also take place in the drop. The experiment was repeated with thin glass plates insulating the drop from contact with the metal of the pole pieces, and $CuSO_4$ and $CuNO_3$ were used, as well as $FeCl_3$. The same type of motion was observed in each case. When the magnet was turned upside down, thus changing the direction of the magnetic field, the motion was observed in the same direction. To test decisively the role of the magnetic field, the magnet was replaced by a replica constructed out of brass.[1] Drops of $FeCl_3$, $CuSO_4$, and $CuNO_3$ were found to "rotate" to the same extent as before, both between layers of Piceïn wax and between glass plates.

Further experiments with the Piceïn-covered permanent magnet showed that there was a very definite acceleration as the light beam was first put on. Progressively dimming the illumination considerably

[1] I am indebted to Professor Leigh Page for this suggestion.

slowed down the motion of the drop. Illuminating the drop from the opposite side definitely changed the direction of motion. The red and infrared radiation was then filtered out by a 2 cm layer of a solution[2] known to pass about 25 per cent. of the visible light. The motion stopped completely within 40 seconds and started again as soon as the filter was removed. When the total intensity of the beam was reduced to 25 per cent. by halving the diameter of a variable diaphragm, the motion slowed down, but did not stop.

From the above results, we can conclude (*a*) that a magnetic field is not necessary for the production of this particular "rotation," (*b*) that this effect is due to the heat radiation of the illuminating light which causes convection currents in the drop (the center being maintained at a higher temperature than the lateral surface, at which evaporation takes place).

No inferences should be drawn from these conclusions as to any other kind of rotation, either in liquids or gases. Further experimental work on these will be published later.

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WHY THE HALO AND THE CORONA DO NOT APPEAR IN THE SAME CLOUD

As explained in any work on atmospheric optics, the halo, of which the most common of its several forms is the rainbow-tinted circle of 22° radius (the full moon subtends half a degree) around the sun or moon, is caused by snow crystals in the air; and the corona, a rather brightly colored ring (sometimes, two —rarely three—concentric rings) usually of two to four degrees radius, about the sun or moon, by tiny water drops.

Both these phenomena, the large halo and the much smaller corona, are often seen in thin clouds (thick clouds scatter the light too much for the rings to remain conspicuous) but never both in the same cloud.

Clearly, then, an intermingling of water droplets, essential to the corona, and ice crystals, necesssary for a halo, can not persist in the air. And this, in turn, is owing to the fact that at every temperature below the freezing point the tendency of water droplets (undercooled, of course) to evaporate is greater than that of ice crystals at the same temperature. The ice crystals, therefore, in a cloud of crystals and droplets, if such a cloud could and did occur, would grow at the expense of the droplets, which quickly would disappear.

At temperatures above the freezing point, snow crystals obviously can not exist, nor, as above explained, can water droplets and snow crystals persist mingled together at temperatures below the freezing point, and even at the freezing point, when the vapor tension over a flat surface of pure water is the same as that over ice, the droplet, owing to an effect of surface tension, still evaporates over to the crystal. Hence, an intermingling of water droplets and ice crystals can not persist at any temperature. Hence, the halo and the corona never appear simultaneously in the same cloud.

In this connection it is interesting to note that, according to tables in Dorsey's "Properties of the Ordinary Water Substance," the difference between the vapor tension of water and that of ice at the same temperature has its maximum value, an amount sufficient to sustain a 0.2 mm column of mercury or equal to a pressure of five pounds per square yard, at around 10° F., a common temperature of the air at halo levels.

W. J. HUMPHREYS

SCIENTIFIC BOOKS

ALGEBRA AND TRIGONOMETRY

College Algebra and Trigonometry, A basic integrated course. xii + 324 pp. By FREDERIC H. MILLER. John Wiley and Sons. 1945. $3.00.

MANY colleges require a year of college algebra and trigonometry as preparation for subsequent study of analytic geometry and the calculus. Some of these colleges may prefer that this college algebra and this trigonometry be intimately merged in some significant way. If so, they will wish to give careful consideration to Mr. Miller's new book.

The reviewer has little interest in a merger of this sort; and, although convinced that much unhappiness in analytic geometry and the calculus is attributable to a poor grasp of algebra, he sees no reason to insist —as so many colleges do insist—that analytic geometry and the calculus shall be withheld until the student shall have acquired so wide an acquaintance with algebra or so rigorous a training in it as this book demands. Nevertheless, the reviewer does have an interest to see that every program, whether traditional or novel—and Mr. Miller's program is a mixture of both—shall have a fair chance to prove its worth; and no program can have this chance until embodied

[2] Handbuch der Physik, Vol. XIX, "Herstellung und Messung des Lichts." Berlin, Julius Springer, publisher, 1928.

in a good book. The reviewer considers this to be a truly excellent book of the sort that the author intends.

It is clear from the preface, and from the body of the book as well, that the student is expected to have had more than one year of algebra in the secondary school and to have studied in high school at least enough trigonometry to have met the various methods of solving oblique triangles.

The main theme of the book is algebraic. The author succeeds in merging the trigonometry in this algebraic pattern by emphasizing the analytic aspects of the trigonometry. Not until the fourteenth chapter does the student meet logarithmic computation and the logarithmic solution of triangles, and then somewhat as asides following upon the discussion of exponential and logarithmic functions and equations.

The final chapters of the book, the fifteenth and sixteenth, set forth the usual ideas concerning rational integral equations, permutations, combinations and probability. The discussion of Descartes's Rule includes complete exposition of the modification "or less by an even integer."

A listing of the contents of the earlier chapters will suffice to give the pattern the author is following. First, number systems, in order to motivate the adoption of the basic assumptions and definitions of algebra. Then, in Chapter 2, variable, functions, graphs. Chapter 3 begins with the general angle and radians, followed by right triangle and polar coordinates. (Remember, the student is supposed to have studied a bit of trigonometry in high school. If he hasn't, he is not likely to appreciate this book.) Chapter 4 considers algebraic identities, conditional equations; then trigonometric identities and equations. (Trigonometric equations appear again in Chapter 9, under equations in quadratic form, and in Chapter 12, under inverse functions.) Systems of linear equations and determinants—no trigonometry—make up Chapter 5. Chapter 6 treats the trigonometric functions of several angles. The remaining chapters, dealing with mathematical induction, complex numbers, progressions, inequalities and functional variation, tend to bear out the author's claim that this book is indeed an integrated course in algebra and analytic trigonometry.

Only one slight blemish: the reviewer does not agree that permuting the letters in the Law of Cosines, proved for the side opposite an acute angle, serves also to establish this law for the side opposite an obtuse angle. Nevertheless, he is glad to cite this text as a practically perfect example of book-making. The exposition throughout, the exercises and the practical aspects of the book all appear to be very fine indeed.

RALPH BEATLEY

ABNORMAL PSYCHOLOGY

Textbook of Abnormal Psychology. By R. M. DORCUS and G. W. SHAFFER. Third edition. Baltimore: The Williams and Wilkins Company. 1945. $4.00.

THIS revision of a text-book which is widely used in colleges and universities brings it up to date in respect to the materials presented, while preserving the virtues of the earlier editions. The authors do not present their topics from a single, selected point of view; but give the diverse views of various authors on points which are theoretical or controversial. While the fact that the reviewer disagrees with the authors on some points is immaterial, four items may be given critical attention in this brief review.

Although the text as a whole makes it evident that most theories in the field of abnormal psychology and psychiatry are devoid of experimental foundations, the popular theory adopted by the authors to the effect that in an epileptic seizure the patient is unconscious (p. 290) needs critical examination. In some cases it can be demonstrated experimentally that in the critical phase of a convulsive seizure, the epileptic is conscious, perceptually conscious at least, although his perceptual field may be restricted in scope; but after the seizure is over, he may have retrograde amnesia for the seizure-period.

The theory adopted in the text—that a psychoneurosis affects only a part of the "personality," while a psychosis affects the whole "personality" (p. 354)—is, of course, a rationalization, that is, it is an attempt to interpret rationally something which is basically irrational. One who adopts this rationalization would have to admit that every psychosis commences as a neurosis; which destroys the distinction claimed. He would have to ignore the existence of neurotics who are as completely disorganized as are many who are classed as psychotics. He would have to ignore also the fact that psychiatrists differ as to whether certain cases are neuroses or functional psychoses. The distinction actually seems, like Topsy, to have "just growed up."

The theory that the primary cause of involutional melancholia is dysfunction of the sex-glands is adopted by the authors by implication, if not explicitly (p. 351); a theory which ignores the high probability that the decrease in secretion of the sex-hormone may be only a predisposing cause in some cases and a precipitating cause in others, the primary cause being psychological in all cases. In every case the reviewer has examined, the psychological cause or causes of the mental feature of the disorder have been readily discernible. The probability is indicated by the occurrence of the mental disorder in some cases several years before the menopause, and by the absence of mental disorder at the menopause in the majority of women.

Two commendations are in order: one is for the sparing use of the term "personality," which is used only in presenting the views of writers who depend upon the term in one or more of its several meanings; the term not appearing in the subject-index at all. The authors, it is obvious, do not endorse what has been called the "personality racket," which in recent years has become a substitute for psychology. One might wish, however, that the authors had indicated that the term can be eliminated from statements in which it occurs; or be replaced by simple terms such as "person" and "personal," with improvement in clarity and definiteness.

The brief discussion of introversion—extroversion (p. 338), presents a thesis which is in agreement with the commercialized tests for detection of introverts and extroverts, and the approved method of scoring those tests, although it is not in accord with the definitions commonly given for extroversion and introversion. This thesis would have been worth expanding into greater detail.

This is not a book for casual reading; but as a text-book, and a book of reference, the wealth of digested materials, and the unusually critical attitude of the authors make it invaluable. The bibliography is extensive, containing 833 titles, to all of which references are made in text; while the author-index and the subject-index are satisfactorily competent.

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TROPICAL MEDICINE

Manual of Tropical Medicine. Prepared under the auspices of the Division of Medical Sciences of the National Research Council. By THOMAS T. MACKIE, GEORGE W. HUNTER, III and C. BROOKE WORTH. 727 pp., including 287 illustrations. W. B. Saunders Company. 1945.

THE present war has taken thousands of the members of our armed forces to far distant lands. In these unfamiliar surroundings and with new experiences, many of the letters home, particularly from those individuals stationed in the tropics, contain weird descriptions of horrible diseases seemingly widespread among the natives: tropical diseases, more to be feared than the enemy. These reports have aroused considerable apprehension in the family circle and have been too often the basis for articles in the lay press. In general the writers are referring to advanced stages of diseases not necessarily maladies indigenous only to the tropics, since primitive people, if they seek medical attention at all, rarely do so in the early stages of sickness. It is most difficult to delimit from the broad field of medicine the scope of tropical medicine. Those diseases which have their greatest incidence in hot, humid climates, and those which are greatly influenced in clinical appearance and prognosis by such an environment fall under the designation "tropical medicine."

In 1942 Dr. Richard Strong prepared a revision of Stitt's "Diagnosis, Prevention and Treatment of Tropical Diseases." These two volumes became at once the standard text-book in this field. The need for a more concise presentation of the subject was envisioned and the authors of the present volume, all colleagues of Dr. Strong in the Army Medical School, undertook the task. The appearance of this manual in the series of military handbooks sponsored by the National Research Council is most timely.

In arranging the contents of the manual, the text was condensed and augmented with tables, summaries and charts, thus making available an unusual wealth of material. The authors have had a unique opportunity not only to prepare an authoritative manual, but to sense the needs of students entering the field of tropical medicine, because of their association with the Army Medical School. In addition to this group, the manual is to be highly recommended for those who wish to familiarize themselves with the subject in a somewhat more general way.

MALCOLM H. SOULE

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